USING MACHINE LEARNING TO ESTIMATE SURVIVAL CURVES FOR TRANSPLANT PATIENTS RECEIVING AN INCREASED RISK FOR DISEASE TRANSMISSION DONOR ORGAN VERSUS WAITING FOR A STANDARD ORGAN

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by

Ethan Joshua Mark

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To those in need of a lifesaving organ transplant

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LIST OF SYMBOLS AND ABBREVIATIONS

BBN	Bayesian Belief Network
C-index	concordance index
CDC	Centers for Disease Control and Prevention
EPTS	Estimated Post Transplant Survival
HBV	Hepatitis B
HCV	Hepatitis C
HIV	Human Immunodeficiency Virus
IRD	Increased Risk for Disease Transmission
IVDU	intravenous drug use
KDRI	kidney donor risk index
KPS	Karnofsky Performance Score
LYFT	Life Years from Transplant
MSE	mean square error
NAT	nucleic acid testing
OPTN	Organ Procurement and Transplantation Network
PHS	Public Health Service
PIRF	permutation importance from random forests
PLD	Partial Likelihood Deviance
PMM	predictive mean matching
RMSE	root mean square error
RSS	Recipient Risk Score
STAR	Standard Transplant Analysis and Research

UNOS	United Network for Organ Sharing
σ	standard deviation

SUMMARY

In 1994, the Centers for Disease Control and Prevention (CDC) and the Public Health Service (PHS) released guidelines classifying donors at risk of transmitting human immunodeficiency virus (HIV) through organ transplantation. In 2013, the guidelines were updated to include donors at risk of transmitting hepatitis B (HBV) and hepatitis C (HCV). These donors are known as increased risk for disease transmission donors (IRD). Even though donors are now universally screened for HIV, HBV, and HCV by nucleic acid testing (NAT), NAT can be negative during the eclipse phase, when the virus is not detectable in blood. In part due to the opioid epidemic, over 19% of organ donors were classified as IRD in 2014. Despite the risks of disease transmission and associated mortality from accepting an IRD organ offer, patients also face mortality risks if they decline the organ and wait for a non-IRD organ. The main theme of this thesis is to build organ transplant and waitlist survival models and to help patients decide between accepting an IRD organ offer or remaining on the waitlist for a non-IRD organ.

In chapter one, we introduced background information and the outline of the thesis. In chapter two, we used machine learning to build an organ transplant survival model for the kidney that achieves greater performance than the model currently being used in the U.S. kidney allocation system. In chapter three, we used similar modeling techniques and simulation to compare the survival for patients accepting IRD kidney offers vs. waiting for non-IRD kidneys. We then extend our IRD vs. non-IRD survival comparisons to the liver, heart and lung in chapter four, using different models and parameters. In chapter five, we built a model that predicts how the health of a patient changes from waitlist registration to

transplantation. In chapter six, we utilized the transplant and waitlist survival models built in chapters three and four to create an interactive tool that displays the survival curves for a patient receiving an IRD organ or waiting for a non-IRD organ. The tool can also show the survival curve if a patient chooses to receive a non-IRD organ immediately. We then concluded with a discussion and major takeaways in chapter seven.

CHAPTER 1. INTRODUCTION

In 1994, the Centers for Disease Control and Prevention (CDC) and the Public Health Service (PHS) released guidelines classifying donors at risk of transmitting human immunodeficiency virus (HIV) through organ transplantation (1). In 2013, the guidelines were updated to include donors at risk of transmitting hepatitis B (HBV) and hepatitis C (HCV). These donors are known as increased risk for disease transmission donors (IRD) (2). Even though donors are now universally screened for HIV, HBV, and HCV by nucleic acid testing (NAT), NAT can be negative during the eclipse phase (the time during early infection when a virus is not detectable in blood). In part due to the opioid epidemic, over 19% of organ donors were classified as IRD during in 2014 (2). Many organ recipients may have to decide between accepting an IRD organ offer or remaining on the waitlist for a non-IRD organ. Despite the risks of disease transmission and associated morbidity and mortality from accepting an IRD organ offer, a patient also has mortality risks if they decline the organ and wait for a non-IRD organ.

The main theme of this thesis is to build organ transplant and waitlist survival models and to help patients decide between accepting an IRD organ offer vs. waiting for a standard organ.

1.1 Using Machine Learning and an Ensemble of Methods to Predict Kidney Transplant Survival

In chapter two, we built a kidney transplant survival model for the general kidney population. The proposed model achieved better performance, measured by Harrell's

concordance index (3), than the Estimated Post Transplant Survival (EPTS) model (4) used in the U.S. kidney allocation system, when evaluated on the same dataset. The model has a five-year concordance index of 0.724 (in comparison, the concordance index is 0.697 for the EPTS model, the state of the art currently in use). To build our model, we used a combination of machine learning techniques including random survival forests and a Cox proportional hazard model. We further produced a ranking of the top variables that are predictive of kidney transplant survival, which include recipient age, recipient diabetes and kidney diagnosis.

1.2 Using Machine Learning and Simulation to Estimate Survival Curves for Hepatitis C Negative Transplant Patients Receiving an Increased Risk for Disease Transmission Donor Kidney Versus Remaining on the Waitlist

In chapter three, we used similar modeling techniques that we used in chapter one, to build transplant survival models for an HCV negative recipient receiving a kidney from an IRD donor, receiving a kidney from a non-IRD donor, and a waitlist survival model for waiting on the kidney waitlist. Using our models, we simulated 20,000 different recipient and donor scenarios and compared the survival for a patient accepting an IRD kidney offer or waiting for a non-IRD kidney offer at a later date for different wait times, including the mean (672 days), half the mean, and one standard deviation (666 days) above the mean wait times from the data. We found that those who received an IRD kidney had, on average, a 0.74% higher (absolute difference) 5-year survival probability than if they waited for one day and received a non-IRD kidney. As the waiting time increased, the benefit for receiving an IRD kidney also increased. Recipients who received an IRD kidney had, on average, a 3.75% higher 5-year survival probability than those who waited for 672 days (the average

wait time in our data) and then received a non-IRD kidney. Further, we built a simple equation to estimate the benefit of receiving an IRD kidney for a particular set of recipient and donor characteristics. As IRD organs have found to be underutilized, these results can help clinicians, researchers and patients access the risk of receiving or declining IRD kidneys.

1.3 Using Machine Learning to Estimate Survival Curves for Patients Receiving an Increased Risk for Disease Transmission Heart, Liver, or Lung Versus Waiting for a Standard Organ

In chapter four, we used similar but different modeling and simulation techniques than in chapter three, to build transplant and waitlist survival models and compare the survival for patients accepting IRD organ offers or waiting for non-IRD organs for the heart, liver, and lung. Based on 20,000 simulations, the recipients had, on average, higher 5-year survival probabilities receiving an IRD organ versus waiting for one day and receiving a non-IRD organ (within 1.33%) for all three organs. The 5-year survival probabilities of heart, liver, and lung recipients who accepted IRD organ offers increased on average by 11.56%, 13.2% and 8.92%, respectively, compared to receiving a non-IRD organ after an average wait time (191, 249, and 227 days respectively). We also developed a simple equation to estimate benefits of receiving an IRD heart, liver and lung versus waiting for a non-IRD organ, for a particular set of recipient/donor characteristics.

1.4 Predicting a Patient's Functional Status at Kidney Transplantation Based on Information at Waitlist Registration

In 2016, there were over 100,000 patients waiting for a kidney transplant in the United States (5). With median waiting times of 3.6 years (based on those that entered the waitlist in 2009) (5), it is important to understand if and how the functional status of a patient may change while on the waitlist, e.g., in evaluating the tradeoffs between accepting an offer for a deceased donor organ versus remaining on the waitlist. Recorded both at registration and at the time of transplantation, the patient's functional status is measured using the Karnofsky Performance Score and takes on values ranging from 0-100 in increments of 10 (6,7). In chapter five, using machine learning techniques, we built a generalized additive model to predict a patient's functional status at transplantation based on information known at the time of waitlist registration. The model's predictions result in an average root mean squared error of 13.05 based on 20 random cross-validation samples of 80% training data and 20% out-of-sample data, from a total sample size of 273,205 transplant records. In comparison, predicting that the functional status remains the same at transplantation as the status at registration, results in an average root mean squared error of 14.68. To our knowledge, this is the first model that predicts how a patient's functional status changes from waitlist registration to transplantation. We also found that diabetes, functional status at registration, UNOS region, and the year placed on the waiting list, most likely impact potential changes in functional status.

1.5 Organ transplant decision support tool

In chapter six, we utilize the transplant and waitlist survival models we built in chapters 3 and 4 to create an interactive tool that displays the survival curves for a patient receiving an IRD organ or waiting for a non-IRD organ. The tool allows the user to enter

custom characteristics of the recipient and donor. The tool can also show the survival curves if a patient chooses to receive a non-IRD organ immediately.

1.6 Conclusion

In chapter seven we conclude the thesis with a discussion and the main take-aways from our work.

CHAPTER 2. USING MACHINE LEARNING AND AN ENSEMBLE OF METHODS TO PREDICT KIDNEY TRANSPLANT SURVIVAL

2.1 Introduction

In 2013, the Organ Procurement and Transplantation Network (OPTN) adopted a new kidney allocation system using the Estimated Post Transplant Survival (EPTS) score (4,8). Other kidney transplant survival models such as the Recipient Risk Score (RSS) (9) and Life Years from Transplant (LYFT) (10), have also been proposed by researchers. These techniques use a Cox proportional hazards model, which estimates the probability of a recipient's post-transplant survival over a given time horizon (11). The Cox proportional hazards model is the most widely used model for kidney transplant survival estimation (12). Additional models include a Bayesian Belief Network (BBN) that was used to predict kidney graft failure (13).

We took a different approach, and used an ensemble of methods including random survival forests constructed from conditional inference trees. Our approach first clusters the data (e.g., into cohorts) and then chooses a model that achieves the best performance for each cluster. The advantage of combining different models to predict kidney transplant survival is that different models may work better than others on different cohorts of the data. We assessed the predictive accuracy of our proposed model using various metrics, including Harrell's concordance index (C-index) (3), which is the percentage of patient pairs correctly "ranked" by the model based on their post-transplant survival duration in a

given timeframe. The C-index for the proposed model is better than that of the EPTS model and other kidney transplant survival models proposed recently in the literature (4,10,12). The results of the model applied to kidney transplant data are presented here, but the approach can be applied to other organs as well.

2.2 Data

The dataset was provided by the United Network for Organ Sharing (UNOS) and consists of recipients who underwent kidney transplant surgery in the U.S. from 1987 to 2014 (14,15). The data includes both living and deceased donors, pediatric and adult recipients, and censored observations. An observation is censored when it does not record a transplant recipient's survival duration after surgery; in these censored observations, the date of the last follow-up is recorded. All data in this study were fully anonymized prior to access by any of the authors. More information on the UNOS data and instructions for researchers to request this data can be found at https://unos.org/data/.

2.2.1 Data preparation

In 2003, the UNOS board of directors instructed the Kidney Allocation Review Subcommittee to review the kidney allocation system (8). Hence, we tested the following hypothesis: There is a statistically significant difference between the survival curves of recipients who underwent a kidney transplant before and after 2002. A log-rank test and visual inspection of the survival curves verified the significant difference (Figure 2-1 and Table A-1) (16). Moreover, starting in 2012, a new allocation system was proposed that used the kidney donor risk index (KDRI) in addition to the EPTS model (17). Therefore, in the analysis we used data that includes all kidney transplants performed between January

1, 2002 and December 31, 2011. Observations after 2012 would not have a 5-year post-transplant window at the time of this study. 5-year or longer time horizons for kidney transplant survival models have often been used in the literature (12,17,18).

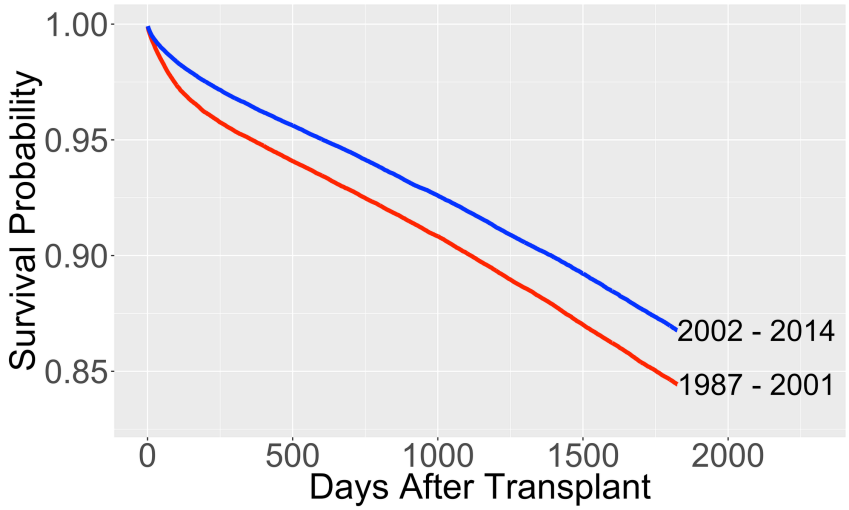

Figure 2-1: Survival probabilities of different transplant cohorts. The survival probabilities are calculated from the Kaplan-Meier estimate.

There were 163,199 observations available during the chosen ten-year time period with 487 variables. We removed variables not present in more than 95% of the observations unless they were identified as important in the previous literature (19-21). In the latter case we removed variables not present in more than 80% of the observations. We also removed variables that were recorded twice, or were known only after the kidney transplant. The resulting data set had 73 variables.

The following approaches were used in addressing the issue of missing data: (i) imputation by predictive mean matching (PMM), and (ii) removing missing data for non-

categorical variables. In approach (ii), we labeled missing data for categorical variables as 'unknown' and removed the non-categorical observations with missing data. Variable selection and all other analysis was carried out using approach (ii), unless specified otherwise. We cross-validated our proposed predictive model using both approaches. When cross-validating our final predictive model with approach (ii), 17% of the data were removed.

Table 2-1: Study inclusion/exclusion criteria.

Inclusion/exclusion criteria	Years of data	Number of observations
Historical kidney transplants with a recorded number of days until last follow-up after surgery or time to death. Observations without a censored status were not considered.	January 1, 2002 and December 31, 2011	163,199

2.2.2 Grouping categorical variables

In the data, some of the categorical variables have a large number of possible values. For example, the variable kidney diagnosis, has 75 different possible values. To avoid overfitting and large model variance, we used the approach described in Text A-1 and illustrated in Table A-2 to group different values of the variable together. The values grouped together have a similar effect on the hazard function, controlling for relevant variables. Following this approach, we decreased the number of different kidney diagnosis values from 75 to 8.

2.3 Methods

2.3.1 Variable selection

For variable selection, we first used the Breiman-Cutler permutation importance measure for random survival forests to rank the variables in order of variable importance (22). Harrell's concordance index was used to measure the error rate for assessing the decrease in accuracy when permuting each predictor variable in the permutation importance calculation.

Recipient age was ranked as the most important variable by permutation importance on the entire dataset. Hence, we decided to split the data into age-based cohorts and produced two separate rankings of variables, one ranking for older recipients and one for younger recipients. This allowed us to build two predictive models for the different cohorts. To find the split value for recipient age, we built 100 survival decision trees (23,24), each with one split using only recipient age. Each decision tree finds the recipient age that gives the best binary split of two groups based on parameters suggested by Strobl et al. (25). The average split value for the 100 trees was 48.7 years. Hence, rounding up to 50, we performed variable selection separately for transplant recipients aged 50 and under (cohort 1), and recipients aged 51 and older (cohort 2). The average 5-year survival probabilities are 93% and 80% for cohorts 1 and 2, respectively, based on the Kaplan-Meier (26) estimate. Figure 2-2 and Figure 2-3 depict the top ten variables for cohorts 1 and 2, respectively, based on random survival forests permutation importance.

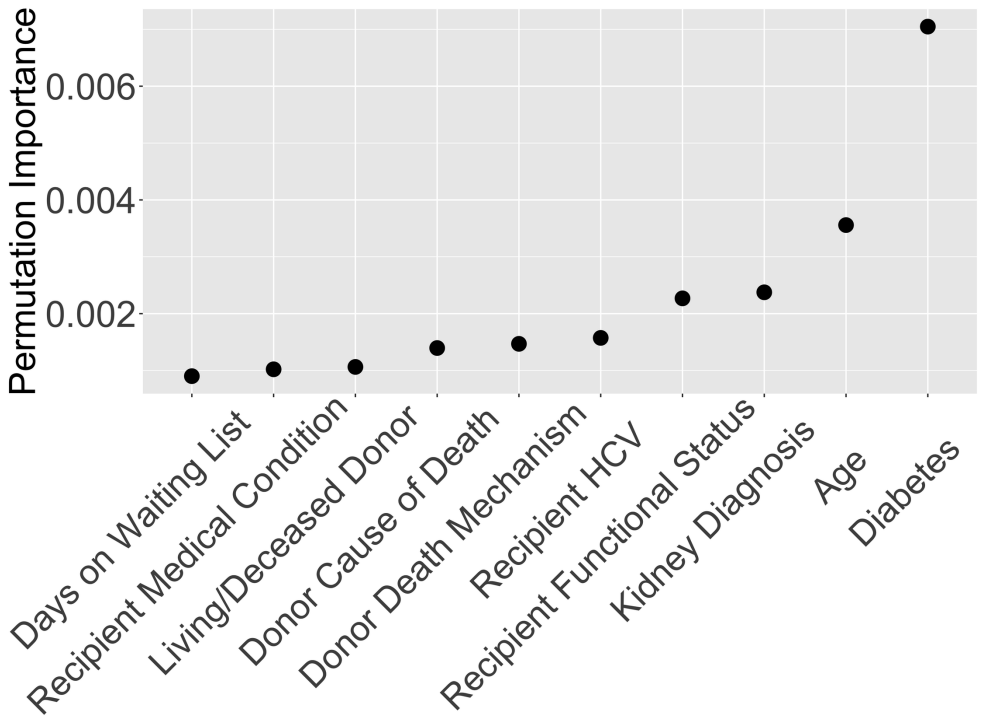

Figure 2-2: Variable importance for recipients ages 50 and under based on Breiman-Cutler permutation importance.

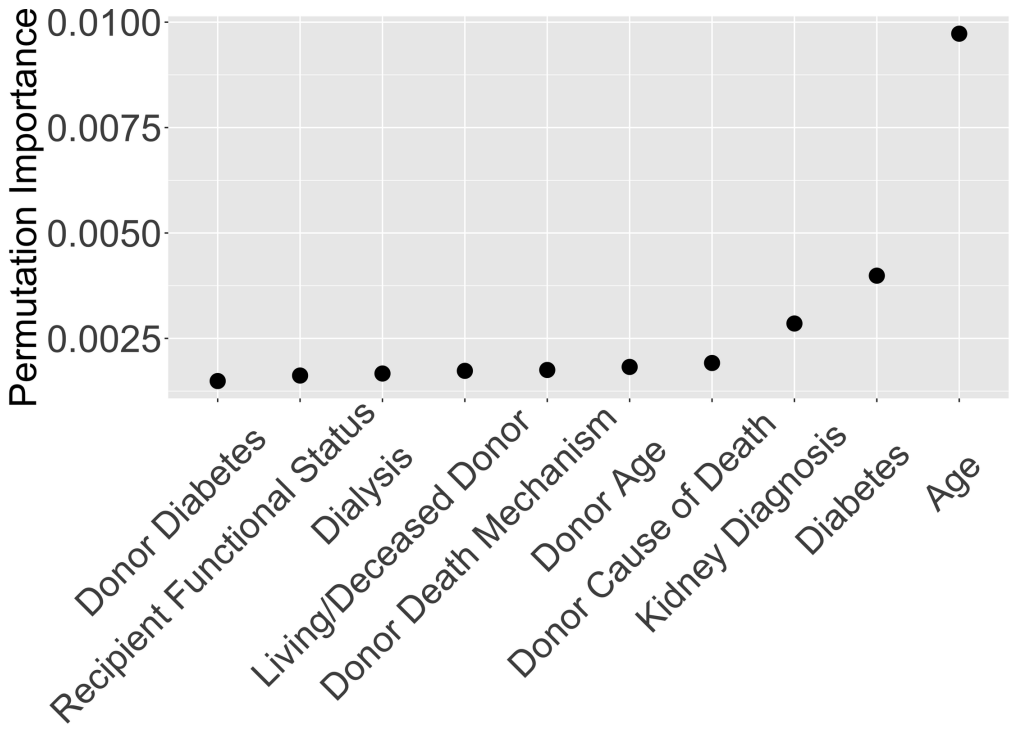

Figure 2-3: Variable importance for recipients ages 51 and older based on Breiman-Cutler permutation importance.

We then used a Cox model regularized with the Lasso (L1) penalty to help determine how many of the top variables to select (27). We used 10-fold cross-validation to determine the optimal Lasso penalty. Figure 2-4 shows the number of nonzero coefficients for different penalty values for cohort 1. The top row represents the number of non-zero coefficients per different values of the Lasso penalty. The vertical line L_0 corresponds to the optimal penalty, which minimizes the Partial Likelihood Deviance (PLD). The line L_σ corresponds to the largest penalty value corresponding to the PLD values within one standard deviation of the minimum PLD. Figure A-1 gives the analogous results for cohort 2. To keep the predictive model simple and minimize the number of variables, we used the L_σ penalty, which has fewer nonzero coefficients than using L_0.

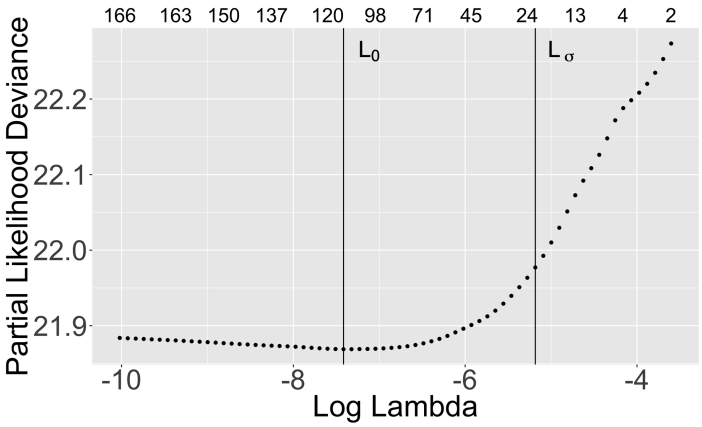

Figure 2-4: Cox Lasso variable selection for recipients ages 50 and under. The top row represents the number of non-zero coefficients per Lasso penalty value, lambda. The vertical line L_0 corresponds to the optimal penalty, which minimizes the PLD. The line L_σ corresponds to the largest penalty value corresponding to the PLD values within one standard deviation of the minimum PLD.

For each cohort, variables that have nonzero coefficients in the Lasso model and which are also among the top 20 variables chosen by permutation importance are included in the predictive model. Table 2-2 lists the final selections of variables for each cohort. Table A-3 provides a description of the variables we used in our proposed predictive survival model. Table A-4 gives the mean values from the data for numeric variables and the percentages of observations for each category for categorical variables.

Table 2-2: Variables in the proposed predictive model. A description of each variable is given in Table A-3.

Cohort 1: ages 50 and under	Cohort 2: ages 51 and older
AGE	AGE

Table 2-2 continued

Cohort 1: ages 50 and under	Cohort 2: ages 51 and older
COLD_ISCH_KI	AGE_DON
CREAT_TRR	ANY_DIAL
DEATH_MECH_DON	COD_CAD_DON
DIAB	COLD_ISCH_KI
DIAG_KI	CREAT_TRR
ETHCAT	DEATH_MECH_DON
FUNC_STAT_TRR	DIAB
HCV_SEROSTATUS	DIAG_KI
HIST_DIABETES_DON	DRUGTRT_COPD
HIST_HYPERTENS_DON	ETHCAT
MED_COND_TRR	FUNC_STAT_TRR
PAYMENTSOURCE_AT_TRANSPLANT	HCV_SEROSTATUS
REGION	HIST_HYPERTENS_DON

2.3.2 Predictive models

For cohort 1, we built a random survival forest model with conditional inference trees as base learners (23,24). We grew a forest with 800 trees and four randomly selected variables considered for each split. Random forest parameters suggested by Strobl et al. (25) were used with a slight modification. We restricted a tree split to occur only if the splitting test statistic exceeded 0.3, instead of guaranteeing the inclusion of all splits. In testing, we found that this allowed the use of smaller trees with the same predictive performance measured by Harrell's concordance index.

For cohort 2, the Cox proportional hazards model achieved a better concordance index than using random survival forests (0.664 vs. 0.655 based on 10 cross-validation

samples of 80% training data and 20% out-of-sample data). Hence for cohort 2, we fit a Cox proportional hazards model. Table A-5 shows the coefficients for the Cox model when it was trained on 100,000 observations.

In the proposed predictive model, we use the combination of random survival forests for cohort 1, and the Cox model for cohort 2. We evaluated the performance of the proposed model compared to other models by two metrics using cross-validation: (i) Harrell's concordance index, and (ii) the integrated Brier score (28). In addition to comparing the performance of our model to the reported performance of the EPTS model (4), we evaluated the EPTS model on the same data that we used for our model. We used PMM for missing data because the EPTS model does not allow for variable inputs to be unknown. We validated our proposed model in multiple ways, using PMM imputation and without imputation.

Our methodology for building the proposed predictive model is described by the following high-level summary:

1. Identify important predictive variables by performing variable selection techniques such as Lasso or permutation importance.
2. Test the performance of multiple predictive models on the data using the variables identified in step 1. Use cross-validation and metrics such as the concordance index to evaluate the performance.
3. Determine the best binary split in the data using methods such as decision trees.

Repeat steps 1–3 for both subsets of the data a specified number of times. The final model consists of combining the predictions from the models that perform best on the different subsets of the data.

The analysis was undertaken using the statistical software R version 3.3.2 as well as several key packages listed in the references (29-35).

2.4 Results

Table 2-3 shows the 5-year Harrell's concordance index and the integrated Brier score for the prosed model using 10 random samples of 80,000 training observations and 20,000 out-of-sample observations. It also reports the performance of a number of other models from the recent literature. Harrell's 5-year concordance index for our proposed model is 0.724 versus 0.69 reported for the EPTS model (4) and 0.697 for the EPTS model applied to the data used for this study. The concordance index of the proposed model is 0.717 when we remove the donor variables and include only the recipient variables. This provides a more direct comparison to the EPTS model since the EPTS model does not use donor variables. The performance of the proposed model was nearly the same when we also validated it using PMM imputation as opposed to validation without imputation.

Table 2-3: Performance of the proposed predictive model compared to other models. Performance from 10 random samples of 80,000 training observations and 20,000 out-of-sample observations for all models except those marked 'Reported', where the metrics shown were provided in the literature for their respective models. *These two predictive models used the variable selection techniques we used for each cohort separately but instead applied to all the data. **Donor variables that were removed were: AGE_DON,

COD_CAD_DON, COLD_ISCH_KI, DEATH_MECH_DON, HIST_DIABETES_DON, and HIST_HYPERTENS_DON.

Table 2-3 continued

Model	5-Year C-index	5-Year integrated Brier score
LYFT Reported (10)	0.680	Not Reported
EPTS Reported (4)	0.69	Not Reported
EPTS Using the Same Cross-Validation Data as the Proposed Model	0.697	Not Calculated
Li et al. (12) Reported	0.700	Not Reported
Cox Model for Both Cohorts*	0.706	0.063
Random Forests for Both Cohorts*	0.718	0.062
Proposed Model without Donor Variables**	0.717	0.060
Proposed Model	0.724	0.061
Proposed Model using PMM Imputation	0.724	0.060

Figure 2-5 and Figure 2-6 illustrate the behavior of our proposed model trained using a random sample of 100,000 observations and validated on 25,000 out-of-sample observations. The solid lines represent the survival predictions and the dotted lines depict the observed Kaplan-Meier estimates for the out-of-sample observations. We also illustrate the model's survival predictions for different values of its variables, holding the remaining variables constant, in Figure A-2 (also see Table A-6 and Table A-7). Table A-8 and Table A-9 present results on the performance of our proposed model at different numbers of days after transplantation and on different categories respectively. Table A-10 gives results for additional tests on the performance of our proposed model and the EPTS model on data without pediatric recipients and living donors. Table A-11 shows the performance of the

proposed model compared to the EPTS model on the general population for each cross-validation sample.

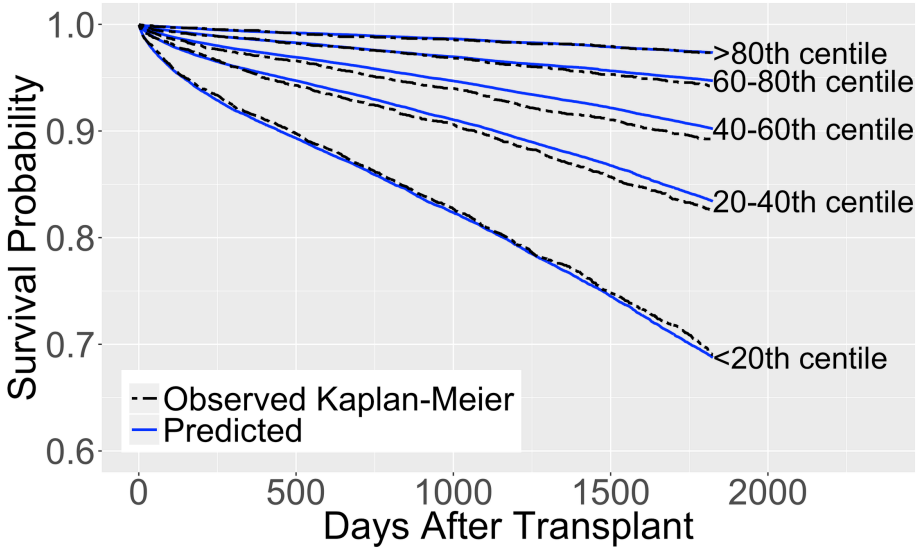

Figure 2-5: Predicted survival of the proposed model. Trained on 100,000 observations and validated on 25,000 out-of-sample observations. The survival curves are separated into 5 groups based on the predicted 5-year survival in the out-of-sample data.

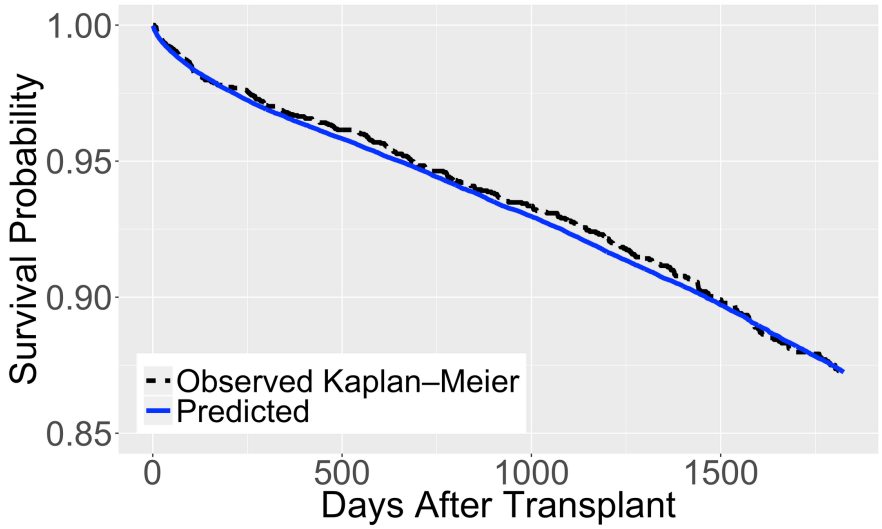

Figure 2-6: Predicted survival of the proposed model for a 'typical' kidney transplant recipient. Trained on 100,000 observations and validated on 25,000 out-of-sample observations. In the out-of-sample data, an observation is considered 'typical' if the values are within one standard deviation of the mean for recipient age, donor age, and cold ischemia time, and the most common values from the data for recipient diabetes, recipient dialysis status, recipient medical condition, and donor hypertension status.

2.5 Discussion

The current kidney allocation system, adopted in 2013, matches the best 20% of kidneys as determined by the KDRI, to the top 20% of potential recipients with the highest predicted transplant survival probabilities, estimated by the EPTS model (17). Improving the predictive performance of kidney transplant survival models can help the kidney allocation system more accurately rank potential recipients based on estimates of post-transplant survival. Table 2-3 shows that our proposed model has a higher concordance index than the EPTS model and other models recently published in the literature, such as the LYFT model and the flexible parametric model proposed by Li et al. (12). Hence, when

considering a random pair of candidates and determining which candidate in the pair has a higher post-transplant survival probability (in a given time frame, e.g., 5 years), our model will result in more correct pair rankings than the EPTS model, and has the potential to significantly improve the matching of organs to recipients. We also found that by using a model that combines different predictive models and variables for different age groups, we achieved better performance than by using the same model and variables for both cohorts.

A comparison of kidney transplant survival models over time shows a concordance index of 0.68 in 2009 for the LYFT model (Wolfe et al., 2009), a concordance index of 0.69 in 2013 for the EPTS model currently used in the kidney allocation system (Clayton et al., 2014), and an index of 0.70 in 2016 from Li et al. (2016). A gain in the index of 0.01 can have a dramatic impact considering that these models are used in the U.S. kidney allocation system, which is responsible for allocating tens of thousands of kidneys per year. Our model yields an improvement in the concordance index of 0.03 over the EPTS model when tested on the same data, which can have a significant impact on ranking kidney waitlist patients by their post-transplant survival more accurately.

Unlike the EPTS model, the proposed model has the flexibility to take into account characteristics of donors; hence, it can help predict which donor-recipient matching can result in the highest post-transplant survival, among several choices. The proposed model can also be used without the donor variables, and still result in a better concordance index than the EPTS model. This can be useful in estimating the survival of transplant recipients before the donor information is known, such as when determining recipient priority in the allocation system.

Our findings suggest that there may be a benefit for building separate models for different cohorts of patients (in this case cohorts separated by recipient age). For example, the variable region, was in the top ten ranked variables for cohort 1 but not for cohort 2. Hence, the impact of region on post-transplant survival is higher for cohort 1 than cohort 2.

The proposed model uses machine learning methods, and although it does not result in a simple equation to predict transplant survival, such methods are straightforward to apply. Further, the proposed model uses 18 different predictive variables versus 4 used by EPTS. While the model complexity could be viewed as a limitation, with the increasing power of computer tools, the model can easily be implemented in practice.

CHAPTER 3. USING MACHINE LEARNING AND SIMULATION TO ESTIMATE SURVIVAL CURVES FOR HEPATITIS C NEGATIVE TRANSPLANT PATIENTS RECEIVING AN INCREASED RISK FOR DISEASE TRANSMISSION DONOR KIDNEY VERSUS REMAINING ON THE WAITLIST

3.1 Introduction

In 1994, the Centers for Disease Control and Prevention (CDC) and the Public Health Service (PHS) released guidelines that classified donors at risk of transmitting human immunodeficiency virus (HIV) through organ transplantation (36). In 2013, the guidelines were updated to include donors at risk of transmitting hepatitis B (HBV) and hepatitis C (HCV) (2). These donors are known as increased risk for disease transmission donors (IRD). Since the guidelines were released, the discard rates have been higher for IRD organs than for non-IRD organs (37). IRD kidneys were found to be one-third less likely to be used for transplantation than non-IRD kidneys with similar characteristics (38). Further, a highly publicized case of HIV and HCV transmission from a single IRD donor in 2007 led to increased fear of IRD organs and reports of lower IRD organ usage (39). In 2009, 19.2% of deceased donor kidneys recovered for organ transplantation were discarded (40).

Prior literature suggests that the risk of infection for IRD organs is very small (41) and that accepting IRD kidney offers rather than discarding them or declining them is associated with increased survival (20,42,43). Increased utilization of IRD organs can reduce the gap between demand (the number of people on the transplant waitlist) and supply (organs available for transplantation) for organ transplants. Between 2003 and 2013, the number of people who either died while on the waitlist or were too sick to receive a kidney transplant exceeded 50,000.

Despite previous literature suggesting the benefits of IRD kidneys, they remain underutilized (44), indicating the need for further research and more definitely establishing the benefits compared to waiting for a non-IRD kidney, with different wait times. In 2017, Volk et al., concluded that "The PHS 'increased risk' label appears to be associated with nonutilization of hundreds of organs per year" (44). With over 19% of deceased donors marked as IRD as of 2014 (2), many individuals may be offered an IRD kidney and face the question of whether to accept the offer. Using machine learning techniques, we built transplant and waitlist survival models, and simulated thousands of different recipient-donor scenarios. We found that in the simulations, patients had, on average, a 0.74% higher 5-year survival probability receiving an IRD kidney than waiting for one day and receiving a non-IRD kidney. As the waiting time increased, the benefit for receiving an IRD kidney also increased. We also quantified the survival benefit for receiving an IRD kidney rather than waiting for different wait times, including the mean (672 days), half the mean and one standard deviation (666 days) above the mean wait times from the data. Further, to our knowledge, we are the first to provide a simple equation to estimate the individual-level benefit of receiving an IRD kidney versus waiting for a non-IRD kidney for a particular set

of recipient and donor characteristics. These estimated survival benefits of receiving IRD kidneys vs. waiting for non-IRD kidneys can help clinicians when informing patients about the benefits and risks of IRD kidneys.

3.2 Methods

To assess the tradeoffs of receiving an IRD kidney instead of waiting for a non-IRD kidney, we developed three separate survival models (using random survival forests) : (i) M_{IRD}: an HCV negative recipient receiving an IRD kidney; (ii) $M_{non\text{-}IRD}$: an HCV negative recipient receiving a non-IRD kidney (after a certain wait time); and (iii) M_{wait}: an HCV negative recipient remaining on the kidney waitlist. We then simulated thousands of different recipient-donor scenarios using our survival models and compared the predicted survival probabilities for receiving an IRD kidney to those of waiting for a non-IRD kidney. From the simulation results, we produced a simple equation to estimate the 5-year survival difference between these two options. The analysis was undertaken using R 3.3.2 (29) and used several key packages listed in the references (29-35).

3.2.1 Data and data preparation

Our dataset, a Standard Transplant Analysis and Research (STAR) file, was obtained from the United Network for Organ Sharing (UNOS) (14,15). The data can be accessed from https://optn.transplant.hrsa.gov/data/request-data/. The data contains transplant records performed in the U.S from 1987 to 2014.

We analyzed patients who entered the waitlist or received a non-multiple organ transplant between August 8, 2000 (the date of the first IRD kidney transplant in the data)

and August 26, 2013 (when the new IRD guidelines were updated). We considered IRD donors using the 1994 guidelines, because at the time of our study, we did not have more than five years of transplantation follow-up data from the most-recent IRD guidelines published in 2013 and many of the 1994 and 2013 criteria overlap. Details regarding the differences in the guidelines can be found in Kucirka et al (2).

We removed variables that had more than 5% of observations missing except if they had been identified as important in several previous studies (20,21,45-47). These important variables were removed only if they had more than 20% of the data missing.

Table B-1 contains a summary of all the variables considered in the analysis after the initial data preparation. We used predictive mean matching multiple imputation to predict the missing data for non-categorical variables, Bayesian logistic regression models for imputation of binary categorical variables, and a Bayesian multinomial regression for imputation of categorical variables with more than two categories (48). We did not use imputation for recipient HCV and donor IRD status, which had 8% and 49% missing data, respectively. We also did not use imputation for donor HCV antibody, HCV RNA, or HCV RIBA status which had 71%, 97%, and 98% missing observations, respectively. However, for these latter variables, missing observations were not removed. Instead, we removed donors that tested positive for these variables when building the predictive models. Imputing HCV status could be misleading because we could not find variables in our dataset that can be used to impute it accurately.

One of the variables, kidney diagnosis, originally contained 74 different categories. To reduce possible overfitting and large model variance, we grouped the number of

different variable values of kidney diagnosis and decreased the number of categories from 74 to 5 (see Table B-2).

When training the models M_{IRD} and $M_{non\text{-}IRD,}$ we considered an observation (a transplant record) to be censored if the recipient's survival time after transplantation was not known. Instead, the date of the last follow-up was recorded. In the model M_{wait}, an observation (a record of a patient waiting for a transplant) was considered censored if the potential transplant recipient was still waiting at the last recorded follow-up time, or was removed from the waitlist for any reason other than death. Observations without either a follow-up time or survival time, and observations without a censored status were also removed from the analysis. Table 3-1 shows the number of observations, the percentage of observations with missing data, the percentage of censored observations, and the number of variables considered before variable selection for the predictive models.

Table 3-1: Data used in the analysis. We included all patients who entered the waitlist or received a non-multiple organ transplant between August 8, 2000 (the date of the first IRD kidney transplant in the data) and August 26, 2013. When building and testing the predictive models, transplants from donors who tested positive for HCV antibody, HCV RNA, or HCV RIBA status were removed. The percent of missing data for each scenario was calculated in the following way: let n be the number of transplant records in the scenario, k be the number of variables used in the predictive model (including censored status and follow-up/death time), and m be the total number of missing values for all variables. The percent of missing data is m/nk.

Model	Scenario	Observati-ons	Missing data	Censored	Variables considered for variable selection	Notes
M_{IRD}	IRD	6679	0.80%	89.8%	98	HCV negative recipients

Table 3-1 continued

Model	Scenario	Observati-ons	Missing data	Censored	Variables considered for variable selection	Notes
						receiving IRD kidneys
$M_{non-IRD}$	Non-IRD	74615	3.10%	87.8%	19	HCV negative recipients receiving non-IRD kidneys
M_{wait}	Waitlist	383742	4.20%	87.0%	16	Patients who are on the waitlist or have received a kidney transplant. We used a random sample of 100,000 observations to train our predictive model.

3.2.2 Selecting variables for survival models

Table B-3 gives a description of the subset of variables used in our predictive models.

We selected which variables to use for each of the predictive survival models, M_{IRD}, $M_{non-IRD,}$ and M_{wait}, respectively, by taking the intersection of the top 10 variables ranked by permutation importance from random survival forests (22), and the variables corresponding to the non-zero coefficients for a Cox Lasso regression model (27) (see Table B-4 for variables among the top 10 in permutation importance also selected by

Lasso). Imputation was used before running the variable selection methods. Once the variables were selected, we used imputation again on a dataset consisting only of the variables used in each predictive model, when training each particular model.

For $M_{non\text{-}IRD,}$ the time a patient remained on the waitlist was included in the model to account for any changes in the health of the patient while on the waitlist. For M_{IRD} and $M_{non\text{-}IRD,}$ we added a variable to the models indicating recipient functional status, to control for differences in the conditions of the recipients receiving IRD organs and non-IRD organs in the historical data. Table 3-2 lists the variables that were used in each of the predictive models.

Table 3-2: Variables used in predictive models. See Table B-3 for a description of the variables. Initially, the variable ON_DIALYSIS was selected for each model, but we replaced it with ON_DIALYSIS_REGISTRATION for $M_{non\text{-}IRD}$ and M_{wait} , and DIAL_TRR for M_{IRD} because some observations of ON_DIALYSIS may have been recorded sometime between waitlist registration and transplantation, instead of at registration.

M_{IRD}	$M_{non\text{-}IRD}$	M_{wait}
AGE	DAYSWAIT_CHRON	DIAB
AGE_DON	DIAB	ETHCAT
CREAT_TRR	ETHCAT	FUNC_STAT_TCR
DIAB	FUNC_STAT_TCR	INIT_AGE
DIAG_KI	INIT_AGE	ON_DIALYSIS_REGISTRATION
DIAL_TRR	ON_DIALYSIS_REGISTRATION	PERIP_VASC
ECD_DONOR	ON_EXPAND_DONOR	PROJECTED_PAYMENTSOURCE_AT_REGISTRATION
FUNC_STAT_TRR	ON_IEXPAND_DONOR	REGION

Table 3-2 continued

HIST_HYPERTENS_DON	PERIP_VASC	TOT_SERUM_ALBUM
	TOT_SERUM_ALBUM	WAITLIST_YEAR
	WAITLIST_YEAR	

3.2.3 Building survival models

Each model, M_{IRD}, $M_{non\text{-}IRD}$ and M_{wait}, predicts the probability of surviving up to a certain timeframe starting from either receiving an IRD transplant or deciding to wait for a non-IRD transplant.

M_{IRD} and $M_{non\text{-}IRD}$ were trained on HCV negative recipients who had a transplant from an IRD and a non-IRD donor, respectively.

M_{wait} was trained on all patients who have either waited for or received a kidney transplant. HCV status was only recorded for those who have had a transplant. Hence, to obtain the survival probability of HCV negative potential recipients on the waitlist, we shifted the waitlist survival predictions from M_{wait} by the following amount at each time point: the average transplant survival probability of HCV-negative kidney recipients at that time minus the average transplant survival probability of all kidney transplant recipients at that time point.

The models were built using random survival forests with conditional inference trees as base learners (24,30,49,50). We used random forest parameters suggested by Strobl et al., for the construction of unbiased random forests suggested by Strobl et al. (25). For each model we used 500 trees, and in each decision tree we only allowed a split

to occur if the splitting test statistic exceeded 0.25. This helped reduce the model size while achieving high accuracy based on Harrell's concordance index (C index) (3).

The random survival forests models were implemented using the 'cforest' function of the R package 'party' and the cox model was implemented using the 'coxph' function in the 'survival' package. The following parameters were used in the 'cforest' function: mtry=ceiling(sqrt([number of variables in model])), ntree = 500, teststat = 'quad', testtype = 'Univ', mincriterion = .25, replace = FALSE, fraction = min(0.632, 40000/[training data size]).

3.2.4 Simulations

Using our three predictive models, we simulated different patient and donor scenarios and compared the survival of a potential recipient either receiving an IRD organ or waiting for a non-IRD organ for different wait times in each scenario. We built our simulations by selecting 20,000 random samples of values from variables chosen for the models including: sampling with replacement from the general kidney transplant population data (see Table B-1 for the distribution of data from the general kidney transplant population) for each numeric variable; and up to the top 3 most-common categories for categorical variables, where the probability of sampling each category was proportional to the data. For variables that were recorded both at transplant and at registration, such as the recipient functional status at transplant and functional status at registration, the simulation sampled the values at transplantation. We also randomly sampled wait times including: 1 day, the mean (672 days in our data set), half the mean, and 1 standard deviation (666 days) above the mean wait time. The simulated scenarios

represent thousands of different patient phenotypes with characteristics representative of common transplant recipients and donors, across four different wait times.

For each simulated scenario, we first computed the survival curve of the patient receiving the IRD organ, using M_{IRD}. We then computed, using M_{wait}, the survival curve if that patient had remained on the waitlist. Finally, we computed, using $M_{non\text{-}IRD}$, the survival curve for the patient receiving a non-IRD organ after the specified wait time of the scenario. We note that for variables recorded both at waitlist registration and at transplantation, M_{IRD} uses the recording at the time of transplant, while M_{wait} and $M_{non\text{-}IRD}$ use the recording at the time of waitlist registration. Because the models do not all use the same set of variables, not all variables in a scenario are used in each model. For example, since we do not know the future (potential) donor characteristics for a patient on the waitlist, there are no donor features used in M_{wait} or $M_{non\text{-}IRD}$.

3.2.5 Benefit equation

After computing the survival curve estimates for each scenario, we ran a linear regression (which we call the benefit equation), regressing the 5-year survival probability for a patient receiving an IRD organ minus the 5-year survival probability of waiting for a non-IRD organ, on the variables used in the simulation (see Table 3-2). We multiply the prediction from this regression (i.e., the estimated difference in the 5-year survival probabilities when receiving an IRD organ vs. waiting for a non-IRD organ) by 100, so that the values, which we call the IRD kidney benefit, are on a scale of -100 to 100. Positive values correspond to the scenarios where receiving an IRD organ versus remaining on the waitlist increases the 5-year survival probability. The coefficients of the benefit equation

can be interpreted as follows: a one unit increase in the value of a variable in the benefit equation is associated with an increase (or decrease) in the IRD kidney benefit, equal to the coefficient for that variable, holding the rest of the variables constant; for a binary categorical variable, the increase (or decrease) in the IRD kidney benefit is instead associated with being in that category as opposed to not being in that category, holding the rest of the variables constant. To test the performance of the benefit equation and the estimated IRD organ benefit, we used 10 random samples of 80% training data and 20% out-of-sample data for validation, comparing the equation's predicted increase/decrease in survival due to receiving an IRD organ to the value predicted from the simulation.

3.2.6 Predicted IRD Transplant Survival for Recipients Who Died on the Waitlist

For patients who died on the waitlist (in our dataset), we predicted their survival probability if they had received an IRD kidney, with average donor characteristics, after remaining on the waitlist for three possible wait times: 50%, 75% and 90% of the waiting time that they remained on the waitlist prior to death. We obtained the survival predictions by first using M_{wait} to predict a patient's probability of survival to a certain time point on the waitlist. We then predicted their survival probability if they had received an IRD kidney using a modification, M'_{IRD}, of M_{IRD}. In M'_{IRD}, we added a variable indicating the wait time to the model; and for all variables in M_{IRD} recorded both at the time of waitlist registration and at the time of transplant, we used the variable at the time of waitlist registration. These modifications allowed the model to control for how the functional status of the patient may have changed from waitlist registration to transplantation. In M'_{IRD}, any information not known until after the waitlist registration, such as the donor variables, was assigned the respective mean values for recipients from the data set who received an IRD kidney. Since

the population who died on the waitlist included both HCV negative and HCV positive patients, we did not exclude HCV positive recipients in $M'_{IRD.}$ We also did not shift their waitlist survival to adjust it to the HCV negative population when using M_{wait}. The training data for M'_{IRD} included 7525 observations, 1.6% missing data and 89.3% censored data. For each patient who died on the waitlist, we recorded the probability that they would have survived longer if they had received an IRD organ after waiting for each of the three different wait times.

3.3 Results

3.3.1 Survival Curves

Example survival probability curves from each of the three models are shown in Figure 3-1. Table B-5 depicts the performance of each model using 10 cross-validation samples. Our IRD, non-IRD, and waitlist models achieve strong performance with a 5-year C index of 0.690, 0.698, and 0.688, respectively, based on 10 cross-validation samples of 20% out-of-sample data. As a comparison, the 5-year C index of the Estimated Post Transplant Survival (EPTS) model used in the U.S. kidney allocation system (4) is 0.682, 0.696, and 0.634, respectively, for IRD, non-IRD, and waitlist survival (based on 10 cross-validation samples on the same data as our models).

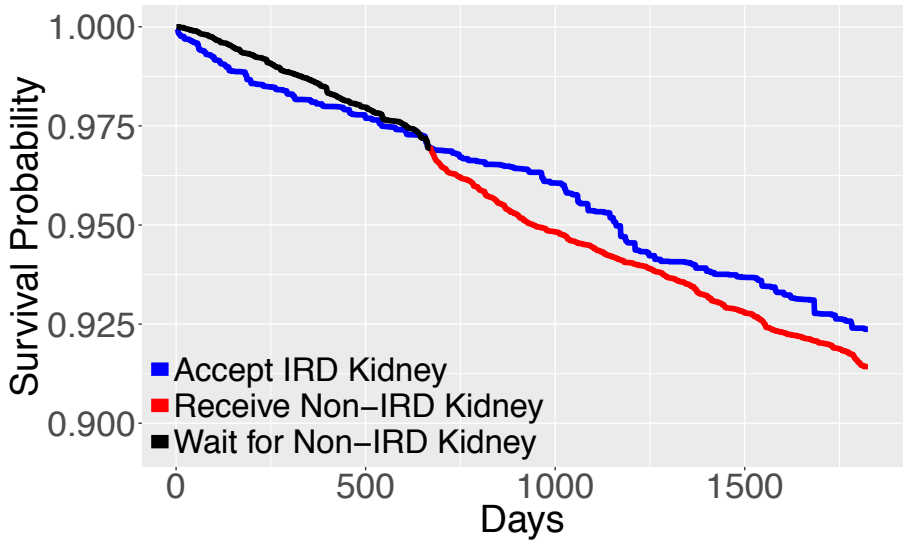

Figure 3-1: Example of survival probability curve comparison between receiving an IRD kidney and waiting for a non-IRD kidney. The predicted survival curves are for a patient who has characteristics of the average numerical variables, and the most common categorical variables used in the predictive models for each scenario. Here, the patient stays on the waitlist for 672 days, the mean waiting time in our data. When waiting for a non-IRD organ, the survival curve starts off as the survival curve for the waitlist. After the waiting time is over, the survival curve then becomes the curve for receiving a non-IRD organ.

3.3.2 Simulation Results

Simulation results suggest that the difference in predicted 5-year survival probabilities between recipients receiving IRD kidneys immediately versus those waiting for non-IRD kidneys depend on the expected wait time (see Table 3-3). In the simulations, 54.95% of recipients had a higher 5-year probability of survival if they received an IRD kidney versus waited for one day and received a non-IRD kidney. Those who received an IRD kidney had, on average, a 0.74% higher 5-year survival probability than if they waited for one day and received a non-IRD kidney. As the waiting time increased, the benefit for receiving an IRD kidney also increased. Recipients who received an IRD kidney had, on

average, a 3.75% higher 5-year survival probability than those who waited for 672 days (the average wait time in our data) and then received a non-IRD kidney.

Table 3-3: Percent of simulations with higher 5-year survival probability of receiving an IRD kidney versus waiting for a non-IRD kidney; and the predicted 5-year survival probability for receiving an IRD kidney minus the 5-year predicted survival probability of waiting for a non-IRD kidney.

Days on waitlist	Percent of simulations with higher 5-year survival probability of receiving an IRD kidney versus waiting for a non-IRD kidney	Predicted 5-year survival probability of receiving an IRD kidney minus the 5-year predicted survival probability of waiting for a non-IRD kidney, averaged over all scenarios
1	54.95%	0.74%
336	63.79%	1.72%
672	73.05%	3.75%
1338	82.02%	9.41%

Figure 3-2 and Figure 3-3 illustrate the results presented in Table 3-3, at different time points after the decision for an average patient wait time, 672 days.

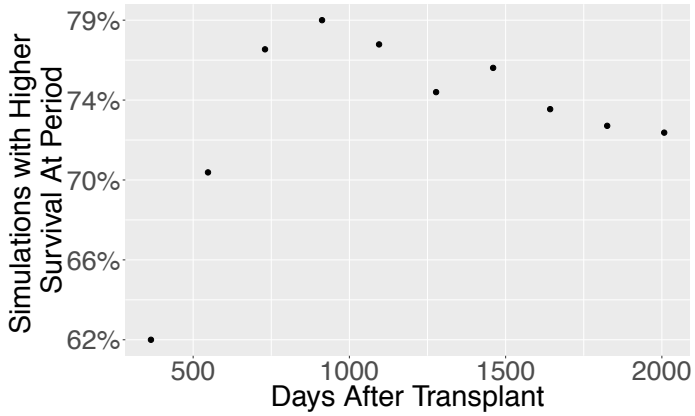

Figure 3-2: Percent of simulations with a higher 5-year survival probability of receiving an IRD organ than waiting for a non-IRD organ at different time points after the decision, with 672 days on the waitlist.

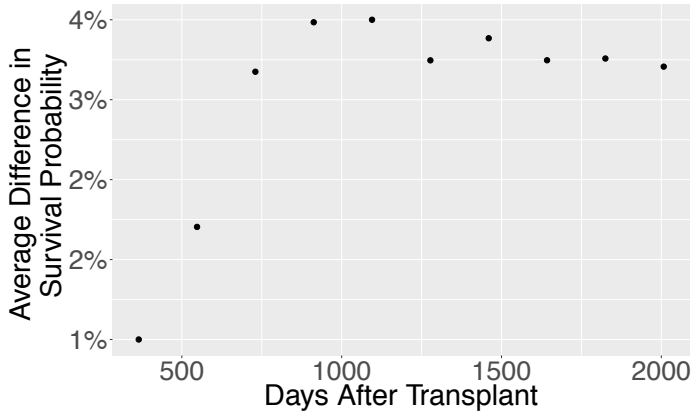

Figure 3-3: The predicted survival probabilities for receiving an IRD organ subtracted by the predicted survival probabilities for waiting for a non-IRD organ, averaged over all simulations with 672 days on the waitlist, for different time points after the decision.

3.3.3 Benefit equation

The coefficients of the regression equation are shown in Table 3-4. These coefficients can be used to determine the increase or decrease in the 5-year survival probability for receiving an IRD kidney instead of waiting for a non-IRD kidney. The average root mean squared error (RMSE) of the 10 cross validations (80% training data and 20% out-of-sample data for each cross-validation) for the equation is 5.10, comparing the equation's predicted increase/decrease in survival probability on a scale of -100 to 100, of receiving an IRD organ, to the value predicted from the simulation (random guessing from a normal distribution with a mean and standard deviation from the simulation results, yields an average RMSE of 11.06). An example of using the benefit equation is shown in Table B-6.

Table 3-4: Benefit equation for the 5-year survival probability of receiving an IRD kidney minus the 5-year survival probability of waiting for a non-IRD kidney. The benefit equation predicts the increase (positive value) or decrease (negative value) in probability (multiplied by 100) of surviving to 5 years with an IRD kidney vs. waiting for a non-IRD kidney. Reference levels for categorical factors: DIAB: No. DIAG_KI: Group_1†. DIAL_TRR: No. ECD_DONOR: 0. ETHCAT: Black. FUNC_STAT_TRR: 60-70 percent performs activities of daily living with some assistance. HIST_HYPERTENS_DON: No. ON_EXPAND_DONOR: 0. ON_IEXPAND_DONOR: 0. PERIP_VASC: No. PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: Medicaid. REGION: 2. †See Table B-2 for categories in this group. Using the coefficients, the equation is: 890.202 + 7.303(DIAL_TRR: Y) + 4.211(PERIP_VASC: Y) + 2.695(DIAB: YES) + 2.106(ON_EXPAND_DONOR: 1) + 1.667(ETHCAT: WHITE) + 1.429(DIAB: NOT KNOWN) + 1.41(ON_IEXPAND_DONOR: 1) + 0.481(PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: MEDICARE) + 0.463(CREAT_TRR) + 0.07(AGE) + 0.007(WAITLISTDAYS) -0.071(AGE_DON) - 0.151(REGION: 5) -0.202(REGION: 3) -0.39(FUNC_STAT_TRR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE) - 0.445(WAITLIST_YEAR) -0.673(ETHCAT: HISPANIC) - 0.694(PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: SOME PRIVATE BY PRIMARY OR SECONDARY) -0.898(FUNC_STAT_TRR: NOT KNOWN) - 1.281(HIST_HYPERTENS_DON: Y) -1.876(DIAG_KI: GROUP_3†) - 2.234(TOT_SERUM_ALBUM) -2.381(ECD_DONOR: 1) -2.846(DIAG_KI: GROUP_5†)

Variable	Coefficients	P-values
(INTERCEPT)	890.202	<0.01
DIAL_TRR: Y	7.303	<0.01
PERIP_VASC: Y	4.211	<0.01
DIAB: YES	2.695	<0.01
ON_EXPAND_DONOR: 1	2.106	<0.01
ETHCAT: WHITE	1.667	<0.01
DIAB: NOT KNOWN	1.429	<0.01
ON_IEXPAND_DONOR: 1	1.410	<0.01
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: MEDICARE	0.481	<0.01
CREAT_TRR	0.463	<0.01
AGE	0.070	<0.01

Table 3-4 continued

WAITLISTDAYS	0.007	<0.01
AGE_DON	-0.071	<0.01
REGION: 5	-0.151	0.08
REGION: 3	-0.202	0.03
FUNC_STAT_TRR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE	-0.390	<0.01
WAITLIST_YEAR	-0.445	<0.01
ETHCAT: HISPANIC	-0.673	<0.01
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: SOME PRIVATE BY PRIMARY OR SECONDARY	-0.694	<0.01
FUNC_STAT_TRR: NOT KNOWN	-0.898	<0.01
HIST_HYPERTENS_DON: Y	-1.281	<0.01
DIAG_KI: GROUP_3†	-1.876	<0.01
TOT_SERUM_ALBUM	-2.234	<0.01
ECD_DONOR: 1	-2.381	<0.01
DIAG_KI: GROUP_5†	-2.846	<0.01

3.3.4 Results from patients who died while on the waitlist

Using M_{wait} and M'_{IRD}, Table 3-5 depicts the percentage of patients who died on the waitlist, who had over a 50% predicted probability of surviving longer if they had received an IRD organ after waiting for 50%, 75% and 90% of the waiting time prior to death while on the waitlist. Table 3-5 shows that most of these patients were more likely to live longer if they had accepted an IRD organ offer.

Table 3-5: Percent patients who died on the waitlist, who would have a greater than 50% predicted probability of surviving longer if they had received an IRD kidney after waiting 50%, 75%, and 90%, respectively, of their total time on the waitlist.

Hypothetical wait time (as a % of the actual time on the waitlist prior to death) before receiving an IRD organ	50%	75%	90%
Greater than 50% probability of surviving longer with IRD organ	99.2%	97.8%	96.4%

3.4 Discussion

We found that in the majority of simulations, recipients had a higher probability of survival if they received an IRD kidney instead of if they remained on the waitlist to receive a non-IRD kidney after the average wait time (672 days). In over half of the simulations, patients had greater survival if they received an IRD kidney versus if they waited for only one day and received a non-IRD kidney. In practice, given the high uncertainty about wait times, the majority of transplant recipients may have a higher survival probability receiving the IRD kidney; in fact, it has been shown that among those patients who received an IRD kidney offer and declined, only 31.0% received a non-IRD kidney within 5 years (43). Our IRD, non-IRD, and waitlist models achieve strong performance compared to using the Estimated Post Transplant Survival (EPTS) model, the state of the art used in the U.S. kidney allocation system (4) when cross-validated on the same data.

While other studies have shown the advantages of increased utilization of IRD kidneys (20,42,43), our study also quantifies the benefit compared to waiting for a non-IRD kidney, at different wait times. To our knowledge, our study is the first to establish a

simple equation that can be used to estimate the benefit of receiving an IRD kidney vs. waiting for a non-IRD kidney for different wait times and recipient/donor characteristics. Our study also differs from previous IRD comparison studies by using random survival forests (versus Cox proportional hazard models) with different variables for the waitlist and transplant survival models, using machine learning variable selection techniques. Using different variables for each model adds an advantage because variables that predict waitlist survival well, may not predict transplant survival well. We further train our survival model for IRD kidneys using only historical IRD transplants, instead of using observations from standard criteria donors given the risk profile of IRD kidneys (20).

One of the reasons why our study likely shows a benefit for IRD kidneys is that transmission of HIV or HCV through transplantation of IRD organs is rare (51). For example, it has been shown that the probability of undetected donor HIV given a negative nucleic acid testing (NAT) screening if the donor exhibited non-medical intravenous drug use (IVDU), one of the IRD donor criteria, one or more days before the NAT screening, is at most 0.92% (51). Other studies also show a low risk of disease transmission (52). Another reason why our simulations likely showed a benefit for receiving the IRD kidneys is that organs recovered from IRD donors are more likely to be from younger and healthier donors (2).

In recent years, treatment regimens for infectious diseases such as HBV, HCV, and HIV have improved (53-55). Hence our survival predictions for recipients of IRD kidneys may be conservative; beyond the time period of our data, the benefit of accepting an IRD organ may be even greater.

In addition to survival probabilities, there are other factors that should be considered when deciding whether to receive an IRD organ, such as costs or the quality of life with a functioning organ. For example, the LYFT kidney transplant survival model used a factor of 0.8 to adjust for quality of life on dialysis as opposed to that with a functioning kidney (21). However our analysis provides strong evidence that utilization of IRD donors may save many people's lives.

CHAPTER 4. USING MACHINE LEARNING TO ESTIMATE SURVIVAL CURVES FOR PATIENTS RECEIVING AN INCREASED RISK FOR DISEASE TRANSMISSION HEART, LIVER, OR LUNG VERSUS WAITING FOR A STANDARD ORGAN

4.1 Introduction

We now expand our survival comparisons in chapter 3, to the heart, liver and lung, using similar but different modeling techniques. For each organ, we computed the survival probability difference for receiving an IRD organ versus the alternative of waiting for a non-IRD organ, at different time points including the mean, half the mean, and one standard deviation above the mean wait time.

Minimal risk for IRD organs and similar survival rates to non-IRD organs have been reported for the heart (56,57), liver (58), and lung (59,60). Further, survival benefits have been reported for accepting IRD organ offers compared to declining them for the kidney (20) and liver (61). Yet, IRD organs continue to be underutilized compared to non-IRD organs (44), and there has been reported fear of using them (39), indicating the need for more research to investigate and disseminate the potential advantages of their use. In 2017, Volk et al., concluded that “The PHS ‘increased risk’ label appears to be associated with nonutilization of hundreds of organs per year” (44).

To our knowledge, this is the first study to quantify the benefit of accepting an IRD heart, lung, or liver, in a simple equation that incorporates individual recipient and donor characteristics, i.e., for a specific patient-organ pair. Further, for the heart, liver, and lung, this study is the first to simulate thousands of different patient scenarios and compare survival probabilities for receiving an IRD organ versus waiting for a non-IRD organ for various wait times.

4.2 Methods

For each of the three organs, we created three separate survival models for HCV-negative recipients (i) M_{IRD}: a patient receiving an IRD organ; (ii) $M_{non\text{-}IRD}$: a patient receiving a non-IRD organ (after a certain wait time); and (iii) M_{wait}: a patient remaining on the transplant waitlist. Hence, we developed 9 survival models in total. For each organ, we then simulated 20,000 different scenarios based on common recipient-donor characteristics and compared the survival if the recipient received an IRD organ immediately or waited for a non-IRD organ. We used the simulation results to develop a linear regression model for each of the 3 organs, with each regression yielding a simple "benefit equation" to estimate the predicted difference in the 5-year survival probability of receiving an IRD organ versus waiting for a non-IRD organ, for a particular set of recipient-donor characteristics. In addition, for patients who died on the waitlist, we estimated survival probabilities for the scenarios if they had received an IRD organ after waiting for 50%, 75%, and 90% of the actual time they were on the waitlist prior to their death.

The computations were performed using the statistical software R version 3.3.2 (29). Several key packages are listed in the references (24,31-35).

4.2.1 Data and data preparation

The data, a Standard Transplant Analysis and Research (STAR) file, was obtained from the United Network for Organ Sharing (UNOS) (14,15). This data can be accessed from https://optn.transplant.hrsa.gov/data/request-data/. The dataset contains records of transplants performed in the U.S. from 1987 to 2014.

For each organ, we used data from patients who entered the waitlist or received a single-organ transplant from the date of the first IRD transplant record in the dataset (June 16, 2001 for heart and liver, and March 30, 2004 for lung) until August 26, 2013 when the IRD guidelines were updated. Given the many common aspects of the 1994 and 2013 guidelines (2), we considered the 1994 guidelines, because at the time of this study we did not have more than 5 years of survival data from transplant records after the announcement of the 2013 guidelines. When building and testing the predictive models, transplants from donors who tested positive for HCV antibody, HCV RNA, or HCV RIBA status were removed, because the risks of bloodborne viral transmission are different for this population. Further, only HCV negative transplant recipients were considered when building and testing the predictive models.

For each organ, we removed variables if they had more than 5% missing data, unless they had been identified as important predictors for recipient survival for that organ in several previous studies (46,62-76). In the latter case, we removed an "important" variable if it had more than 20% missing data. To predict the values of missing data for the variables included in the model, we used predictive mean matching imputation for numerical variables, Bayesian logistic regression for categorical variables with 2

categories, and multinomial Bayesian regression for categorical variables with more than 2 categories (48). We did not use data imputation for recipient HCV status or for donor IRD status (the proportions of missing data for these variables were 10% and 23% for the heart, 11% and 26% for the liver, and 10% and 1% for the lung, respectively); we removed the corresponding observations with missing values when building the models. We also did not use imputation for donor HCV antibody, HCV RNA, or HCV RIBA status (which had over 95% missing data for each organ); however, we did not remove the observations with missing values and instead, removed donors who tested positive. Imputing HCV status could be misleading because we could not find variables in our dataset that can be used to impute it accurately.

One of the variables, patient diagnosis, contained a large number of categories (greater than 30 for each organ). Hence we grouped the values for these categories into 5 larger groups, by combining categories with similar transplant survival after controlling for other factors (Table C-1).

We considered an observation as censored in our transplant survival models (M_{IRD} and $M_{non\text{-}IRD}$) if the transplant record does not have an exact time of death after surgery and instead has the last known follow-up time for which the patient was alive. We considered an observation as censored in our waitlist survival models (M_{wait}) if a patient was still waiting at the last recorded follow-up time, or was removed from the waitlist for any reason other than death. Observations without a censored status or follow-up/death time were removed from the analysis. Table 4-1 shows the number of observations, variables, observations with missing data, and censored observations for the data we used to build the three models for each organ.

Table 4-1: Data used in the analysis. For each organ, we used data from patients who entered the waitlist or received a single-organ transplant from the date of the first IRD transplant record in the dataset (June 16, 2001 for heart and liver, and March 30, 2004 for lung) until August 26, 2013 when the IRD guidelines were updated. When building and testing the predictive models, transplants from donors who tested positive for HCV antibody, HCV RNA, or HCV RIBA status were removed, and for patients that received a transplant, only HCV negative recipients where considered. *We used a random sample of 100,000 observations to train our predictive model for scenarios where the number of observations exceeded 100,000. The percent of missing data for each scenario was calculated in the following way: let n be the number of transplant records in the scenario, k be the number of variables used in the predictive model (including censored status and follow-up/death time), and m be the total number of missing values for all variables. The percent of missing data is m/nk.

Organ	Model	Scenario	Observations	Missing data	Censored	Variables considered for variable selection
Heart	M_{IRD}	IRD	1578	0.7%	79.8%	128
	$M_{non\text{-}IRD}$	Non-IRD	16346	2.7%	78.5%	30
	M_{wait}	Waitlist	38388	0.8%	88.4%	26
Liver	M_{IRD}	IRD	1980	0.6%	82.5%	125
	$M_{non\text{-}IRD}$	Non-IRD	24952	1%	81.3%	30
	M_{wait}	Waitlist	124679*	0.6%	85.4%	26
Lung	M_{IRD}	IRD	1010	0.5%	62.7%	123

Table 4-1 continued

Organ	Model	Scenario	Observations	Missing data	Censored	Variables considered for variable selection
	$M_{non\text{-}IRD}$	Non-IRD	12013	0.4%	60.4%	28
	M_{wait}	Waitlist	19217	0.6%	89.6%	29

4.2.2 Selecting variables for survival models

We selected the variables to use in each of our nine models except for the lung IRD model, by taking the intersection of the top 10 variables chosen by permutation importance using random survival forests (22,49) and the variables corresponding to the non-zero coefficients of a Cox-Lasso model (77). For the lung IRD model, we took the intersection of the top 5 variables (instead of the top 10) chosen by permutation importance and the non-zero coefficients of a Cox-Lasso model, because the lung had a small number of IRD observations. Using too many variables may overfit the model. Harrell's concordance index was used to calculate the difference in error rates before and after in the permutation importance calculation (3). Imputation was used to predict the values of missing data prior to variable selection. Imputation was then performed again using only the variables selected when training the predictive models. The response variable (survival time and censored status), was not used when performing imputation in the out-of-sample data when cross-validating our models.

For M_{IRD} and $M_{non\text{-}IRD}$ for all organ types, we added the variables, recipient functional status at transplantation and recipient age (if it was not already selected by the variable selection methods), to control for differences in the population who received IRD transplants vs. those who received non-IRD transplants. The functional status takes on values ranging from 0 to 100 in increments and gives information on a patient's ability to perform daily tasks and the amount of assistance they need. Because M_{wait} and $M_{non\text{-}IRD}$ are used to predict the survival if a patient chooses to wait for a non-IRD organ, we only considered the variables that are known at waitlist registration (for example, there is no donor variable in M_{wait}) in these models. For $M_{non\text{-}IRD,}$ after using our variable selection method, we added a variable to indicate the time that a patient was on the waitlist because the estimated wait time is an input in our simulation. This variable helps take into account how the health status and variable values of the patient may have changed between registration and transplantation.

Table 4-2 shows the variables selected for each of the nine models. Table C-2 gives a description of the variables used in the predictive models, and Table C-3 shows the variables with the top 10 permutation importance measures that were also selected by Lasso. Table C-4, Table C-5, and Table C-6 give a summary of the variables used in the predictive models for the heart, liver and lung respectively.

Table 4-2: Variables used in the predictive models. See Table C-2 for a description of the variables.

Organ	M_{IRD}	$M_{non\text{-}IRD}$	M_{wait}

Table 4-2 continued

Heart	AGE	CIG_USE	ECMO_TCR
	AGE_DON	DAYSWAIT_CHRON	FUNC_STAT_TCR
	CREAT_TRR	ETHCAT	HGT_CM_TCR
	DEATH_MECH_DON	FUNC_STAT_TCR	INIT_AGE
	DIAG	INIT_AGE	INIT_STAT
	FUNC_STAT_TRR	MOST_RCNT_CREAT	INOTROPES_TCR
	INSULIN_DON	PRIOR_CARD_SURG_TCR	LIFE_SUP
	MOST_RCNT_CREAT	PROJECTED_PAYMENTSOURCE_AT_REGISTRATION	MOST_RCNT_CREAT
	PAYMENTSOURCE_AT_TRANSPLANT	THORACIC_DGN	VAD_DEVICE_TY_TCR
	TRANSFUSIONS	TOT_SERUM_ALBUM	VENTILATOR_TCR
		WAITLIST_YEAR	WAITLIST_YEAR
Liver	AGE	DAYSWAIT_CHRON	EXC_HCC
	ASCITES_TX	DGN_TCR	FUNC_STAT_TCR
	BMI_CALC	DIAB	INIT_AGE
	FINAL_DIALYSIS_PRIOR_WEEK	FUNC_STAT_TCR	INIT_ALBUMIN
	FUNC_STAT_TRR	INIT_AGE	INIT_BILIRUBIN
	INIT_SERUM_CREAT	INIT_MELD_OR_PELD	INIT_INR
	LIFE_SUP_TRR	INIT_SERUM_CREAT	INIT_SERUM_CREAT
	MED_COND_TRR	NUM_PREV_TX	INIT_STAT
	ON_VENT_TRR	PREV_AB_SURG_TCR	LIFE_SUP_TCR
	SGPT_DON	PROJECTED_PAYMENTSOURCE_AT_REGISTRATION	VENTILATOR_TCR
			WAITLIST_YEAR
Lung	AGE	DAYSWAIT_CHRON	CIG_USE
	DIAG	FUNC_STAT_TCR	FUNC_STAT_TCR
	FUNC_STAT_TRR	GROUPING	GROUPING
	GROUPING	INIT_AGE	INIT_AGE

Table 4-2 continued

	HGT_CM_DON_CALC	INIT_BLU_FLG	INIT_O2
	HIST_CIG_DON	INIT_O2	INIT_RLU_FLG
		PROJECTED_PAYMENTSOURCE_AT_REGISTRATION	REGION
		REGION	THORACIC_DGN
		THORACIC_DGN	WAITLIST_YEAR

4.2.3 Building survival models

M_{IRD} and $M_{non\text{-}IRD}$ predict the post-transplant survival and M_{wait} predicts the waitlist survival probabilities (for up to 5 years in our computations). We compared the predictive performance of the Cox proportional hazard model (11) to random survival forests with conditional inference trees as base learners (24,30,49) based on Harrell's concordance index. We used random forest parameters for the construction of unbiased random forests (25). The random survival forest models each used 500 trees, and each decision tree only allowed a split to occur if the split statistic exceeded 0.25. The Cox model performed better or the same across all scenarios except for M_{IRD} for the heart (in which the Harrell's concordance index was 0.005 lower in the Cox model). Hence we built M_{IRD}, $M_{non\text{-}IRD}$ and M_{wait} using the Cox model.

For each organ, M_{IRD} and $M_{non\text{-}IRD}$ were trained on all HCV negative transplant recipients who received that organ from an IRD donor and a non-IRD donor, respectively. For each organ, M_{wait} was first trained on all waitlist patients for that organ, and some of those patients may be HCV positive. Note that HCV status of patients was not recorded in our data at waitlist registration (it was recorded at the time of transplantation). In general,

it is expected that the average difference of the survival probability of an HCV negative versus an HCV positive recipient with the same characteristics (if they had received the same organ) would be positive. Let us denote the post-transplant survival probability difference t days after transplantation between HCV negative recipients, and all recipients (which includes both HCV positive and negative recipients) by Δt. To estimate the waitlist survival for HCV negative patients, we added Δt to M_{wait} at each time point, from the estimated waitlist survival model trained on all patients.

The random survival forests models were implemented using the 'cforest' function of the R package 'party' (24,30) and the cox model was implemented using the 'coxph' function in the 'survival' package (33). The following parameters were used in the 'cforest' function: mtry=ceiling(sqrt([number of variables in model])), ntree = 500, teststat = 'quad', testtype = 'Univ', mincriterion = .25, replace = FALSE, fraction = min(0.632, 40000/[training data size]).

4.2.4 Simulations

For each organ, we generated 20,000 random samples of the following combinations of all variable values used in the predictive models: sampling with replacement from the data (from the general population, without excluding IRD donors and HCV positive recipients or donors; see Table C-4, Table C-5, and Table C-6 for the distributions of the general transplant populations for the heart, liver, and lung respectively.) for each numeric variable; and up to the top 3 most-common categories for categorical variables where the probability of sampling each category was proportional to the data. For each recipient, we chose a random waiting time based on the wait time data

for each organ: either 1 day, half the mean, the mean (191, 249, 227 days for the heart, liver and lung respectively), or one standard deviation (348, 468, 406 days for the heart, liver and lung respectively) above the mean. For variables recorded both at transplantation and at waitlist registration, we used the mean and standard deviation of the values recorded at transplantation. These scenarios represent common characteristics of recipient-donor combinations for the four different wait times.

Using the predictive models M_{IRD}, M_{wait}, and $M_{non\text{-}IRD,}$ for each recipient we compared the survival probabilities of receiving an IRD organ (M_{IRD}) to waiting and receiving a non-IRD organ (M_{wait} followed by $M_{non\text{-}IRD}$).

4.2.5 Benefit equation

For each scenario in the simulation, we calculated the difference between the predicted probability of surviving 5 years after waiting and receiving the non-IRD organ, and the predicted probability of surviving 5 years after receiving the IRD organ immediately. For each of the three organs, we then used a linear regression to estimate the benefit (increase or decrease in 5-year survival probability) from receiving an IRD organ compared to waiting for a non-IRD organ for each recipient-donor pair. We call this model the benefit equation. We multiply the predictions from the equation by 100 so that the values are on a scale of -100 to 100. The values from the equation predict the increase (or decrease) in survival probability, multiplied by 100 to be on a scale of -100 to 100, for receiving an IRD organ vs. waiting for a non-IRD organ for a particular set of recipient and donor characteristics and wait times.

The coefficients of the linear regression can be interpreted as follows: for numerical variables, a variable's coefficient is the recipient's percentage increase/decrease in 5-year survival when receiving the IRD organ compared to waiting for a non-IRD organ, for every one-unit increase in the value of the variable, holding the rest of the variables constant; for a binary categorical variable, the coefficient is the recipient's percentage increase/decrease in 5-year survival when receiving the IRD organ vs. waiting for a non-IRD organ, for being in that category (corresponding to the coefficient) compared to not being in that category, holding the rest of the variables constant. For each organ, we tested the performance of the benefit equation using 10 random samples of 80% training data and 20% out-of-sample data and compared our equation's predicted benefit with the results of the simulations.

4.2.6 Predicted IRD transplant survival for recipients who died on the waitlist

For each organ, we calculated the predicted survival of patients (in our data) who died on the waitlist, if they had instead received an IRD organ with average donor characteristics after waiting for one of three possible wait times: 50%, 75% or 90% of the time that they remained on the waitlist before they died. We first used M_{wait} to compute their survival probabilities on the waitlist. We then used $M'_{IRD,}$ a modification of M_{IRD} to compute their survival probabilities receiving an IRD organ. In $M'_{IRD,}$ for all variables recorded both at transplant and at waitlist registration, we used the variable at registration and we added a variable to indicate the amount of time the patient waited on the waitlist to account for changes in the patient's characteristics and health status between waitlist registration and transplant. We set the value for variables that were only known at transplantation to be the average in our data, because this information was not known yet for the patients on the waitlist. For each organ, these averages were calculated using IRD transplants for that particular organ. Imputation was used to predict the missing values for

the variables with partially missing information. M'_{IRD} was trained on 1760 observations with 0.7% missing data and 79.4% censored observations for the heart, 4029 observations with 6.4% missing data and 78.5% censored data for the liver and 1126 observations with 0.4% missing data and 62.3% censored data for the lung. When training the model for $M'_{IRD,}$ we did not exclude HCV negative recipients because the patients who died on the waitlist included both HCV positive and negative recipients. We also did not shift their survival to adjust it to the HCV negative population when using $M_{wait..}$

4.3 Results

Table C-7 shows the performance of each of the nine models based on ten cross validation samples with 80% training data and 20% out-of-sample data. It also shows the comparison of the predictive models using both the Cox proportional hazards model and the random survival forests model.

4.3.1 Survival curves

Figure 4-1 shows example survival probabilities from our models. In general, for average wait times and characteristics, the survival probabilities are higher for recipients accepting IRD organ offers versus waiting and receiving non-IRD organs.

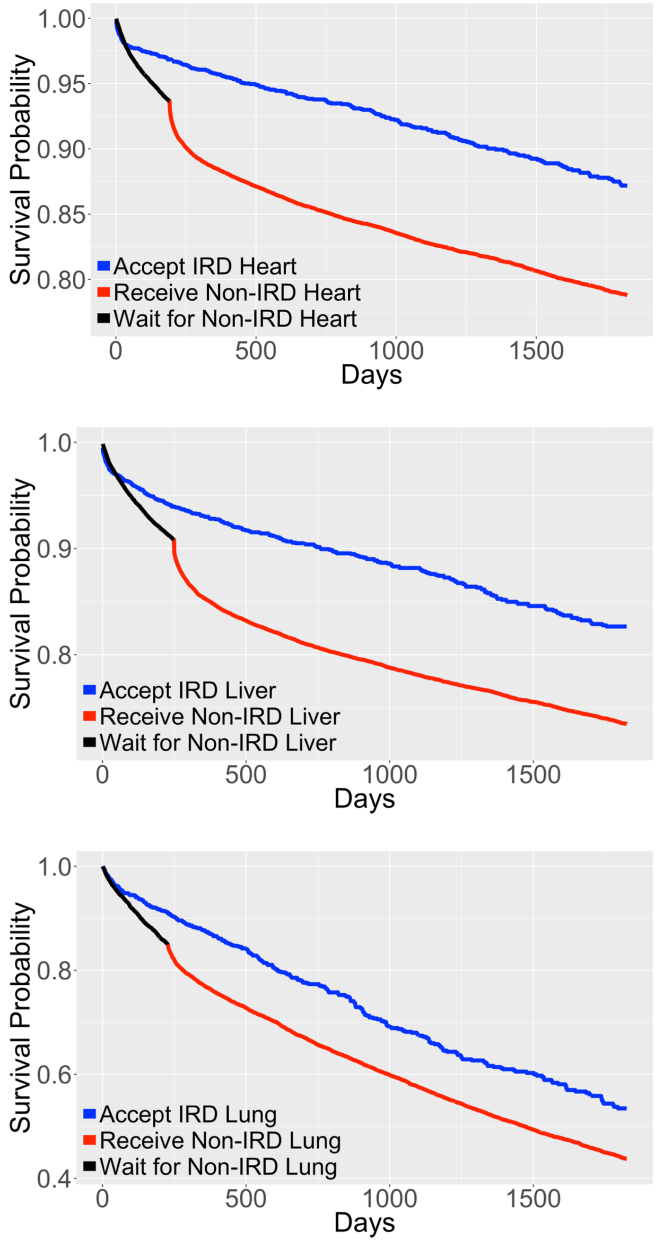

Figure 4-1: Survival probability curve of recipients receiving an IRD organ (in blue) and recipients waiting for a non-IRD organ (in black and red) by organ for the heart, liver and lung. The predicted survival curves are for a patient who has characteristics of the average numerical variables, and the most common categorical variables used in the predictive models for each scenario. The mean waiting times are 191, 249, and 227 days for the heart, liver, and lung, respectively. Before transplantation with a non-IRD organ, the survival curve represents the waitlist survival (in black). After transplantation with a non-IRD organ, the survival curve then becomes the curve for patients who have received a non-IRD organ (in red).

4.3.2 Simulations results

Table 4-3 shows that for all three organs, the majority of scenarios have a higher predicted 5-year survival if a recipient accepts the IRD organ offer versus waits and receives a non-IRD organ, with the difference in survival probabilities being 11.56% for hearts, 13.2% for livers, and 8.92% for lungs, respectively, for average organ waitlist times (191 days for the heart, 249 days for the liver, and 227 days for the lung). The percentage of simulations with a higher survival probability was 84.72% for hearts, 85.91% for livers, and 75.33% for lungs. Longer estimated wait times lead to a greater positive difference in survival probabilities for patients accepting IRD organ offers. Figure 4-2 shows the survival probabilities for IRD organ recipients at time points other than 5-years.

Table 4-3: Percent of simulations with higher 5-year survival probability of receiving an IRD organ versus waiting for a non-IRD organ; and the predicted 5-year survival probability for receiving an IRD organ minus the 5-year predicted survival probability of waiting for a non-IRD organ.

Organ	Days on Waitlist	Percent of simulations with higher 5-year survival probability of receiving an IRD organ versus waiting for a non-IRD organ	Predicted 5-year survival probability of receiving an IRD organ minus the 5-year predicted survival probability of waiting for a non-IRD organ, averaged over all scenarios
Heart	1	55.04%	0.48%
	95 (1/2 mean)	78.14%	7.99%
	191 (mean)	84.72%	11.56%
	539 (1 SD above mean)	90.43%	17.82%
Liver	1	55.98%	1.33%

Table 4-3 continued

Organ	Days on Waitlist	Percent of simulations with higher 5-year survival probability of receiving an IRD organ versus waiting for a non-IRD organ	Predicted 5-year survival probability of receiving an IRD organ minus the 5-year predicted survival probability of waiting for a non-IRD organ, averaged over all scenarios
	124	81.53%	9.18%
	249	85.91%	13.2%
	717	88.19%	21.08%
Lung	1	57.72%	1.15%
	114	71.69%	6.5%
	227	75.33%	8.92%
	633	81.06%	14.69%

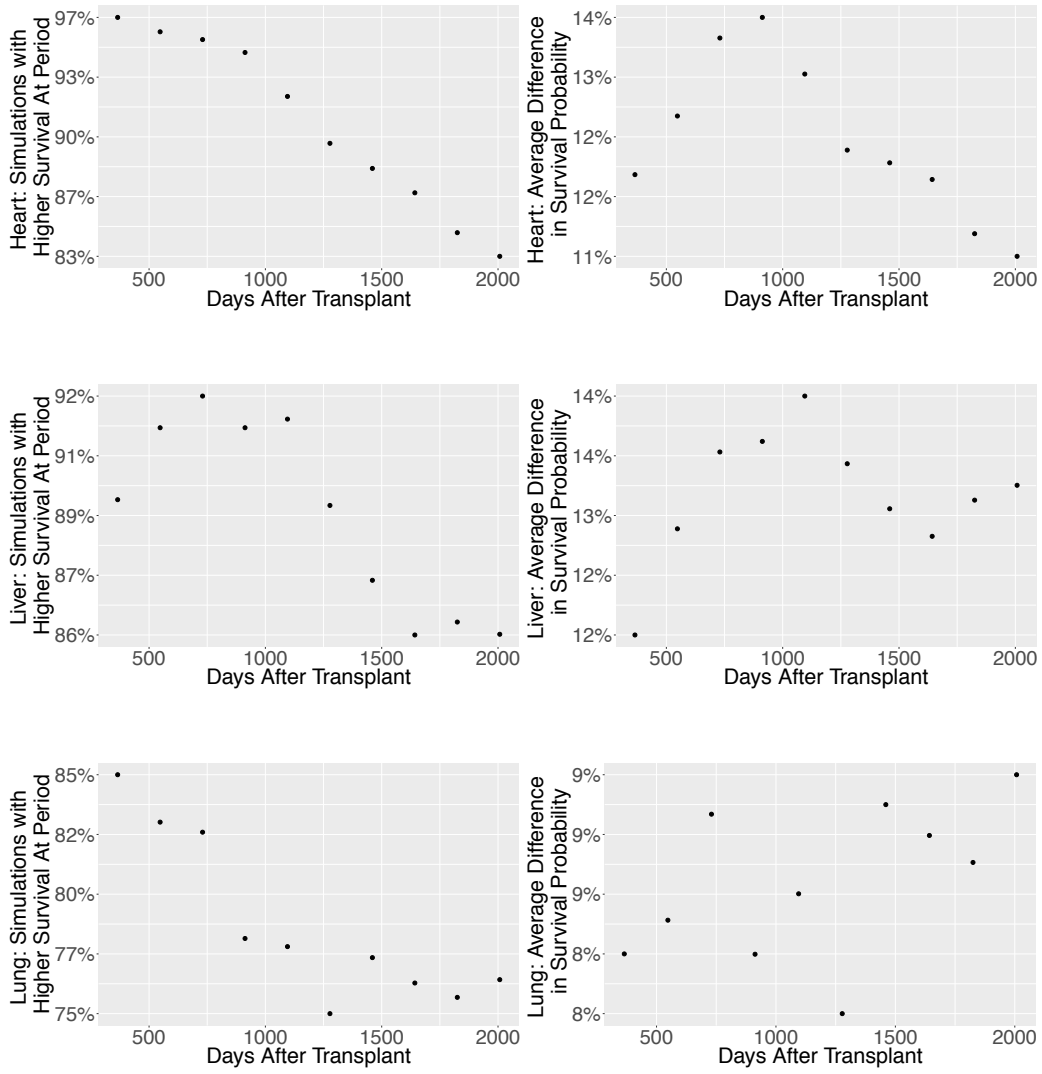

Figure 4-2: Simulation results from Table 4-3 at different time points. On the left: percent of simulations with a higher 5-year survival probability of receiving an IRD organ than waiting for a non-IRD organ at different time points after the decision, with the average wait time for each organ (191 days for the heart, 249 days for the liver, and 227 days for the lung); on the right: the predicted survival probabilities for receiving an IRD organ subtracted by the predicted survival probabilities for waiting for a non-IRD organ with the average wait time on the waitlist, averaged over all simulations, for different time points after the decision.

4.3.3 Benefit equation

Table 4-4 shows the benefit equation built from the simulation results for each organ. Table C-8 shows an example use of the benefit equation for each organ. Table C-9 shows the results of the linear regression used to construct the benefit equation. The root mean square error (RMSE) of testing the benefit equations on the simulation results (comparing our equations' predicted benefit with the results of the simulations) are 5.1, 8.7, and 5.6 for the heart, liver, and lung respectively (in comparison, the RMSE using random guessing from a normal distribution with the mean and standard deviation from the results of the simulation is 20.2, 22.7, and 21.4 respectively).

Table 4-4: Benefit equations for the 5-year survival probability of receiving an IRD organ minus the 5-year survival probability of waiting for a non-IRD organ. The benefit equations predict the increase (positive value) or decrease (negative value) in probability (multiplied by 100) of surviving to 5 years with an IRD organ vs. waiting for a non-IRD organ. See Table C-8 for an example usage of the benefit equations and Table C-9 for the p-values and reference levels for the linear regression used to construct the equation.
*See Table C-1 for categories in this group.

Organ	Benefit equations
Heart	2275.823 + 10.85(ECMO_TCR: 1) + 8.949(PAYMENTSOURCE_AT_TRANSPLANT: SOME PRIVATE BY PRIMARY OR SECONDARY) + 8.203(FUNC_STAT_TRR: NOT APPLICABLE (PATIENT < 1 YEAR OLD)) + 7.824(DIAG: GROUP_4*) + 7.492(INSULIN_DON: Y) + 5.125(PAYMENTSOURCE_AT_TRANSPLANT: MEDICARE) + 4.623(VAD_DEVICE_TY_TCR: LVAD/RVAD/TAH UNSPECIFIED) + 4.501(MOST_RCNT_CREAT) + 4.469(PRIOR_CARD_SURG_TCR: Y) + 4.1(VENTILATOR_TCR: 1) + 2.422(VAD_DEVICE_TY_TCR: NONE) + 1.992(CIG_USE: Y) + 0.772(LIFE_SUP: Y) + 0.461(INOTROPES_TCR: 1) + 0.108(AGE) +

Table 4-4 continued

	0.029(WAITLISTDAYS) – 0.063(HGT_CM_TCR) – 0.214(AGE_DON) – 1.125(WAITLIST_YEAR) – 1.299(DEATH_MECH_DON: STAB OR GUNSHOT WOUND) – 1.964(FUNC_STAT_TRR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE) - 2.334(TOT_SERUM_ALBUM) -2.862(DIAG: GROUP_3*) – 2.914(DEATH_MECH_DON: INTRACRANIAL HEMORRHAGE/STROKE) – 3.424(INIT_STAT: HR: STATUS 1B) – 5.324(TRANSFUSIONS: Y) – 5.508(CREAT_TRR) – 5.688(INIT_STAT: HR: STATUS 2) – 6.45(ETHCAT: HISPANIC) – 6.629(ETHCAT: WHITE)
Liver	1024.296 + 14.262(INIT_STAT: >= 25) + 10.852(EXC_HCC: NON-HCC) + 9.019(FINAL_DIALYSIS_PRIOR_WEEK: N) + 7.795(DGN_TCR: GROUP_4*) + 6.131(FINAL_DIALYSIS_PRIOR_WEEK: Y) + 5.147(NUM_PREV_TX) + 4.976(VENTILATOR_TCR: 1) + 4.442(DGN_TCR: GROUP_3*) + 3.207(DIAB: YES) + 2.877(PREV_AB_SURG_TCR: Y) + 1.724(INIT_MELD_OR_PELD: PELD) + 1.691(INIT_STAT: 18-11) + 1.521(INIT_SERUM_CREAT) + 0.619(LIFE_SUP_TRR: Y) + 0.412(INIT_INR) + 0.392(INIT_BILIRUBIN) + 0.207(AGE) + 0.025(WAITLISTDAYS) + 0.016(SGPT_DON) – 0.38(BMI_CALC) – 0.513(WAITLIST_YEAR) – 1.525(DIAB: NOT KNOWN) - 1.677(PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: MEDICARE) – 2.198(FUNC_STAT_TRR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE) - 2.324(ASCITES_TX: SLIGHT) – 2.616(MED_COND_TRR: NOT HOSPITALIZED) – 3.864(MED_COND_TRR: IN INTENSIVE CARE UNIT) –

Table 4-4 continued

	3.964(ON_VENT_TRR: 1) – 4.201(PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: SOME PRIVATE BY PRIMARY OR SECONDARY) – 4.612(INIT_ALBUMIN) – 5.079(FUNC_STAT_TRR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE) – 8.173(ASCITES_TX: MODERATE)
Lung	1601.523 + 17(GROUPING: C) + 5.642(GROUPING: D) + 3.707(DIAG: GROUP_4*) + 1.708(INIT_O2) + 1.674(REGION: 4) + 0.443(HGT_CM_DON_CALC) + 0.02(WAITLISTDAYS) – 0.111(AGE) – 0.828(WAITLIST_YEAR) – 1.59(FUNC_STAT_TRR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE) - 1.687(FUNC_STAT_TRR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE) – 1.995(CIG_USE: Y) – 2.099(PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: MEDICARE) – 2.436(INIT_RLU_FLG: 1) – 4.904(REGION: 5) – 6.337(INIT_BLU_FLG: 1) – 7.477(PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: SOME PRIVATE BY PRIMARY OR SECONDARY) - 15.121(DIAG: GROUP_3*) – 15.214(HIST_CIG_DON: Y)

4.3.4 Patients who died while on the waitlist

For a patient p who died on the waitlist, let W_p denote the number of days the patient remained on the waitlist until death. Our models predict that over 97% of the patients who died on the waitlist were predicted live longer if each patient p received an IRD organ after waiting for $W_p/2$ days (Table 4-5). For those 97% of patients, if they had

received an IRD organ, the post-transplant survival probability would be >50% after W_p days. Table 4-5 also shows the percent of patients that were predicted to live longer if they had received an IRD organ after a wait time of $0.75W_p$ and $0.9W_p$ days.

Table 4-5: Percent of potential recipients who died on the waitlist, with a greater than 50% predicted probability of surviving longer if they had received an IRD organ. The results of the table are shown by organ type and by days on waiting list, after waiting 50%, 75% and 90% of the waiting time that they actual died on the waitlist.

Hypothetical days on waitlist until receiving IRD organ as a percentage of the time the patient actual died on the waitlist.	50%	75%	90%
Greater than 50% probability of surviving longer with IRD heart	98.9%	98.4%	98.1%
Greater than 50% probability of surviving longer with IRD liver	97.5%	96.3%	95.8%
Greater than 50% probability of surviving longer with IRD lung	98.1%	97.8%	97.9%

4.4 Discussion

For all three organs, the majority of simulated patients had a higher predicted survival accepting an IRD organ offer compared to waiting for a non-IRD organ with average wait times. These simulated scenarios represent typical recipient and donor characteristics. For the heart, liver and lung, the simulation had, on average, higher 5-year survival probabilities receiving an IRD organ versus waiting for one day and receiving a non-IRD organ (within 1.33%). As estimated wait times increase, the difference also increases, suggesting that patients who are likely to wait for longer times would benefit more from receiving an IRD organ (versus waiting and receiving a non-IRD organ later).

For any of the three organs, an estimated increase (or decrease) in 5-year survival probability for receiving an IRD organ for a particular set of recipient and donor characteristics, and particular wait time, can be quickly found using the benefit equations.

For the heart, liver and lung, previous studies compared the survival of IRD organs to non-IRD organs using a retrospective analysis that divided the population into two groups. While a large scale simulation, where comparisons were made for thousands of scenarios, was conducted for the kidney (20), to our knowledge, this has not been performed for the heart, liver and lung.

Further, to our knowledge, this is the first study to develop a simple equation that estimates the difference in the survival probabilities for receiving an IRD organ versus waiting and receiving a non-IRD organ (heart, liver, or lung) for a given recipient-donor pair.

There are several reasons behind the benefits of receiving an IRD organ. The risk of undetected infection resulting in transmission is very small. The estimated risk of undetected HIV infection by serologic screening among IRD donors was found to be 1/11,000 for HIV and 1/1,000 for HCV (78). According to the same study, NAT screening was projected to have even lower undetected risks. In addition, advances in treatment for HIV and HCV have resulted in improved mortality (79,80). Another reason why our simulations likely showed a benefit for receiving the IRD organs is that organs recovered from IRD donors are more likely to be from younger and healthier donors (2).

A limitation of our analysis is that our simulations cannot estimate whether there are survival probability increases (or decreases) for receiving IRD organs beyond a 5-year

horizon. As the post-transplant time horizon increases, the number of patients with available survival data decreases. It is possible that receiving an IRD organ for a particular scenario may result in a higher 5-year survival probability, but waiting for a non-IRD organ may result in a higher survival probability many years later, although this appears unlikely given advances in HIV and HCV treatment (79,80).

Another limitation is that we have a relatively small sample size of data from IRD heart, liver, and lung transplants (e.g., compared to kidney transplants). However, we still have over 1,000 observations for IRD transplants for each organ, and by conducting 20,000 simulations of recipient/donor scenarios for each organ, we were able to predict and assess the survival benefits for significantly more scenarios; hence, our study complements other studies that focus on retrospective data analysis. Third, because treatment for HIV and HCV has improved, our models, which use data prior to 2013, are likely to be "conservative," i.e., under-estimate the survival probabilities for IRD organ recipients. With current advances in HIV and HCV treatments, we expect that the survival benefits for receiving IRD organs would be even higher.

While a comparison of survival probabilities between IRD and non-IRD organs is important, there are other factors to take into account when deciding whether to receive an IRD organ such as cost and quality of life. The quality of life for a patient on the waitlist is likely lower compared to a recipient with a functioning transplant (21). Patients and physicians might overestimate the risks of receiving an IRD organ and better tools for accurately discussing the risks during informed consent are needed (38,44,81). This study's comparison between receiving an IRD heart, liver, and lung and waiting for a non-IRD

organ can help physicians, patients, and researchers assess whether to accept or decline an IRD organ.

CHAPTER 5. PREDICTING A PATIENT'S FUNCTIONAL STATUS AT KIDNEY TRANSPLANTATION BASED ON INFORMATION AT WAITLIST REGISTRATION

5.1 Introduction

In 2016, the number of patients on the kidney transplant waiting list exceeded 100,000, roughly double the number in 2002 (5,82). With median waiting times exceeding 3.6 years based on patients that entered the waitlist in 2009 (5), it is important to understand how the functional status of a patient changes during the potentially long time period between waitlist registration and transplantation. A patient's pre-transplant functional status is an important predictor of post-transplant survival for the kidney (6,83,84) and other organs (85,86). Functional status has also been shown to predict the likelihood of receiving a kidney (87) and survival in chronic kidney disease (88). Understanding potential changes in functional status while on the waitlist is also important while deciding whether to accept a deceased donor organ offer or remain on the waitlist. We built a machine learning model to predict the functional status of a patient at transplantation, given information known about the patient at waitlist registration.

We identified important predictive variables and provided a comparison of the predictive performance for different models.

5.2 Methods

We first cleaned and prepared the data, and then performed variable selection to determine variables that are predictive of functional status at transplantation based on information known at waitlist registration . We then applied machine learning and a variety of statistical methods to build a model that predicts a patient's functional status at transplantation. The analysis was performed using R 3.3.2 (29).

5.2.1 Data and data preparation

The dataset, a Standard Transplant Analysis and Research (STAR) file, was obtained from the United Network for Organ Sharing (UNOS) (14,15). The data can be accessed from https://optn.transplant.hrsa.gov/data/request-data/. The data contains records for transplants performed in the U.S from October 1, 1987 to March 31, 2014, with 658,697 patients waitlisted for a kidney transplant.

We used all records where a patient was originally registered and listed for, and eventually received a kidney transplant. We did not consider transplant records if (i) the patient's functional status at transplantation was missing or not known; or (ii) the functional status at either registration or transplantation was considered "not applicable." After data cleaning, the resulting dataset contained 273,205 transplant records.

Variables with more than 25% missing data were removed from the analysis, unless they were found to be predictive variables of waitlist or transplant survival based on several previous research articles (20,21,45-47). In the latter case, variables were removed if they had over 50% missing data. Variables not known until after the waitlist registration and variables that stopped being recorded in 2014, were also removed from the analysis.

Table D-1 contains a description of the variables considered in the analysis and Table D-2 provides summary statistics of the variables.

To deal with missing data, we used predictive mean matching multiple imputation for non-categorical variables, Bayesian logistic regression for binary categorical variables, and Bayesian multinomial regression for categorical variables with more than two categories (48) prior to variable selection. After variable selection, we used missing value imputation by chained random forests (89) with only the variables selected for our predictive models, when building and cross-validating the predictive models. When using imputation for the out-of-sample observations, we did not include functional status at transplantation to impute missing values for the other variables, because functional status at transplantation will not be known for new data we want to predict.

The patient's functional status is measured using the Karnofsky Performance Score (KPS) and takes on values ranging from 0-100 in increments of 10 (6,7). It is recorded both at the time of registration and transplantation ("FUNC_STAT_TCR" and "FUNC_STAT_TRR", respectively, in the dataset). The functional status is based on a patient's ability to perform daily tasks and the amount of assistance they need. For example, the scores range from "10% - Moribund, fatal processes progressing rapidly", to "100% - Normal, no complaints, no evidence of disease', with values in the middle range such as "50% - Requires considerable assistance and frequent medical care". During data preparation, we grouped multiple categories for the same increment of 10 into one group. For example, "100% - Normal, no complaints, no evidence of disease" and "100% - Fully active, normal" were both grouped into the group "100". In addition, three of the original categories did not correspond to a numerical score in the data and only had a description;

hence, we grouped them into the most-similar category we could identify based on the descriptions. Table D-3 lists the original categories for the variables and the resulting grouped categories after data preparation.

Figure 5-1 illustrates the distribution of functional status values at registration and at transplantation. We find that for 66% of the patients, the functional status remains the same between registration and transplantation. The functional status decreases for 22% of the patients and increases for 13% of the patients from registration to transplantation (see Figure 5-2). Figure 5-3 shows the distribution of functional status at transplantation based on the status at registration. It illustrates how on average, patients with a functional status at registration above 80 have a lower functional status at transplantation, while patients with a functional status at registration below 80 have a higher status at transplantation.

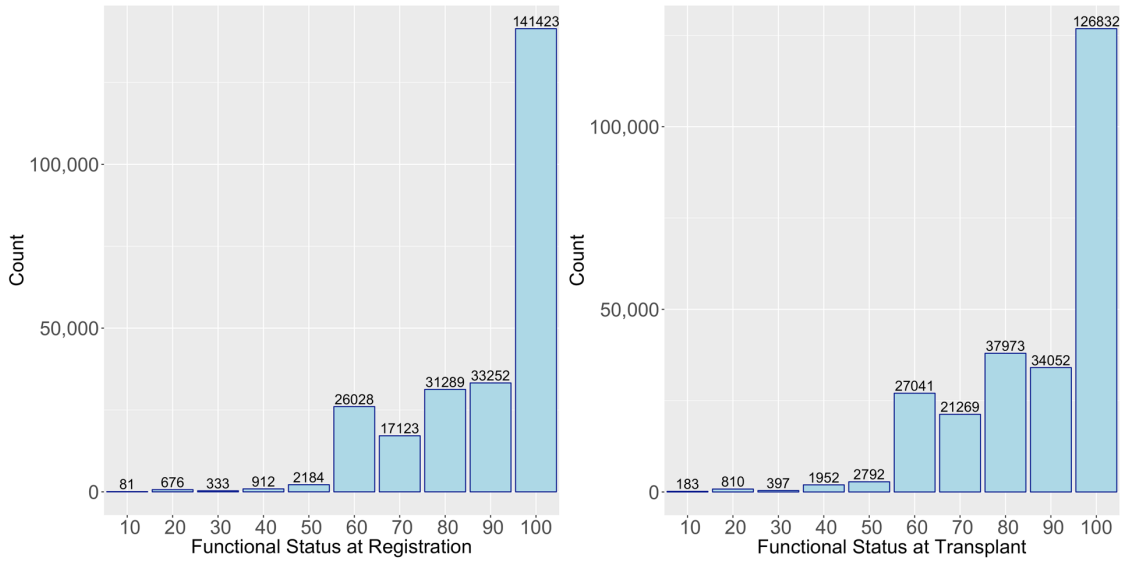

Figure 5-1: Distribution of functional status recorded at registration and at transplantation for patients who have both values recorded in the data.

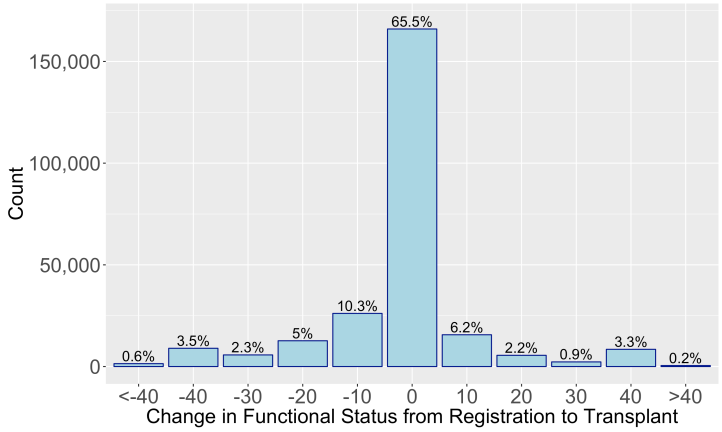

Figure 5-2: Distribution in change of functional status from registration to transplantation for patients who have both values recorded in the data.

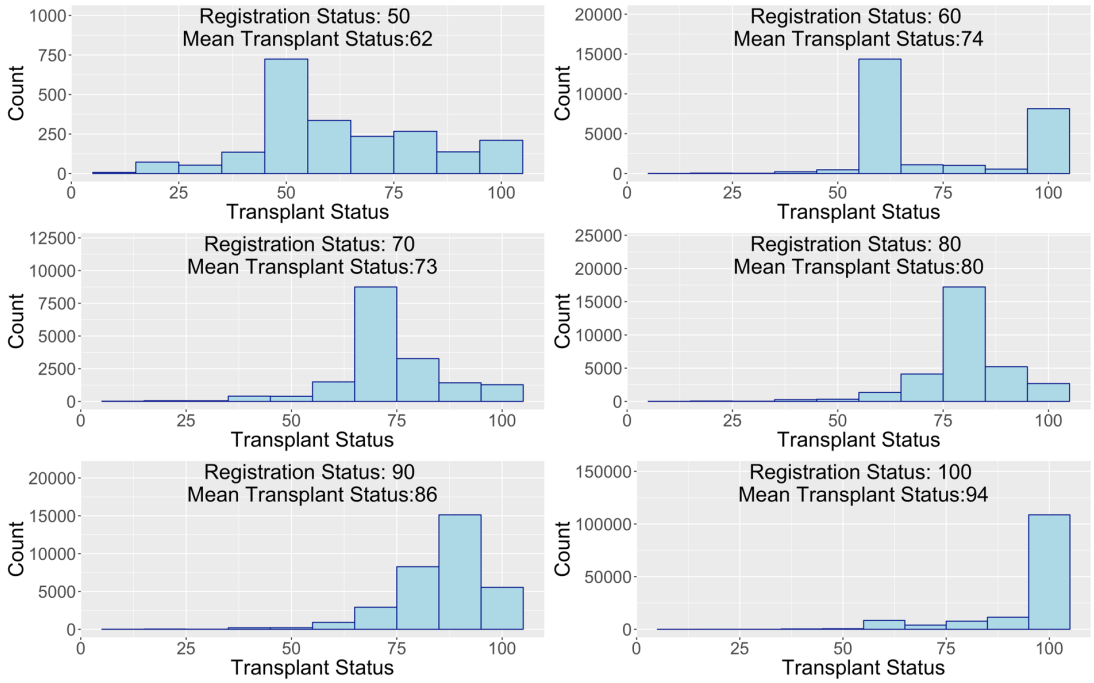

Figure 5-3: Distribution of functional status at transplantation by functional status at registration.

Table 5-1: Study inclusion/exclusion criteria

Inclusion/exclusion criteria	Years of data (transplant date)	Number of observations
Patients who received a kidney transplant with a recorded functional status at transplantation. Patients who were not originally listed to receive a kidney or patients who received a kidney-pancreas transplant were removed	October 1, 1987 to March 31, 2014	273,205

5.2.2 Selecting variables for the predictive models

We utilized three different variable selection methods, namely, (i) group Lasso (90), (ii) permutation importance from random forests (PIRF) (91) focusing on the top 10 variables, and (iii) Multivariate Adaptive Regression Splines (MARS) (92). When using group lasso, we grouped all binary variables for a particular categorical variable into the same group. These methods identified three sets of variables as candidates for the predictive model.

To consider interaction effects between variables, we applied two additional variable selection approaches: (iv) we used the joint-VIMP approach to identify interaction effects by focusing on the top 15 variables chosen by PIRF (22). We then constructed this fourth set of variables by including the top 5 interaction effects (ranked by the absolute difference between their paired importance and their sum of individual variable importance measures) and the top 10 variables chosen by PIRF. (v) We applied MARS with all the variables originally selected by MARS and their pairwise interactions.

We refer to our five sets of variables sets as (i) Lasso, (ii) PIRF 10, (iii) MARS, (iv) PIRF interactions, and (v) MARS interactions.

5.2.3 Building predictive models

The predictive models we compared are: linear regression, linear regression with a Box-Cox transformation (93), a generalized additive model with penalized cubic regression splines, and a Gaussian link function (94,95), random forests (91), gradient boosting with regression trees (96), support vector machines (97), and feed-forward neural networks with a single hidden layer (98). For each of the five sets of variables chosen by

the variable selection methods, we tested the performance of our predictive models using 20 cross-validation samples of 80% training data and 20% out-of-sample observations.

In the generalized additive model with interactions, we used the tensor product for pairs of variables selected by the interaction variable importance methods. In addition to approaching the problem from a regression framework, we also used a model from a classification framework, and used gradient boosting with a softmax (99) objective function, where each increment of ten on the functional status scale was treated as a separate class.

When implementing support vector machines and neural networks, we normalized the data as suggested by Graf et al. (100), and LeCun et al. (101). We used Z-score normalization, where the means and standard deviations for each variable in both the in-sample and out-of-sample data were taken from the training data set. For the random forests, gradient boosting, support vector machines and neural network models, we used cross-validation on the training data to select hyper-parameters for the models using a grid search. We rounded the resulting predictions for all the models to the nearest 10 to be on the same scale as the true functional status values, which are recorded in increments in 10.

We also built a stacking model that combined the predictions of the generalized additive model, gradient boosting, support vector machines, and neural networks model. When building the stacking model, for each cross-validation, we split our data into 3 sets: A training set consisting of 64% of the data, a validation set consisting of 16% of the data (obtained by splitting our original training set into two sets of 80% and 20% portions), and a testing set consisting of 20% of the data. We trained the 4 models on the training set and

made predictions on the validation set. We then ran a linear regression, where we regressed the functional status at transplantation in the validation set, on the predictions from each of the 4 models on the validation set. The coefficients resulting from the linear regression for each prediction gave weights to the predictions from each model. Using these weights, we then made predictions on the testing data and combined them into one final predicted value.

To speed up the computations of running all the cross-validations for each model, we trained some of the models on smaller random samples of the training data. We tuned (performed cross-validation on the training data to select hyper-parameters) the gradient boosting with softmax, support vector machines, and neural network models on 50,000, 100,000 and 100,000 observations, respectively; we trained these models on 100,000, 100,000 and 150,000 observations without interactions and 100,000, observations when using interactions. In addition, we trained the generalized additive model with 100,000 observations when using interactions.

For each cross-validation sample, we used the following metrics to assess predictive accuracy: (i) RMSE: root mean squared error, (ii) MSE: mean squared error, (iii) σ MSE: the standard deviation of MSE for the ten cross-validation samples. (iv) A10: if the true value is X, the percent of predictions that are within (X-10 to X+10 inclusive) and (v) A20: if the true value is X, the percent of predictions that are within (X-20 to X+20 inclusive), Note that RMSE penalizes inaccurate predictions more severely compared to A10 or A20; for example, if the true value of an observation is 70, A10 penalizes a prediction of 50 the same as a prediction of 10. Nevertheless, A10 or A20 may be of interest to physicians or patients in practice.

As a benchmark, we considered a model that predicts the functional status to remain the same between registration and transplantation (recall that 66% of the observations in the data have the same functional status at registration and transplantation, and hence, this simple benchmark model has a reasonable predictive power).

After comparing the performance of the predictive models, we took the best performing model by RMSE, and removed the variable "ON_DIALYSIS" for our final predictive model. In the data, "ON_DIALYSIS" may have been recorded after the waitlist registration and at another time period on the waitlist instead (and hence it would not be consistent with our goal of using information only known at waitlist registration to predict transplant functional status).

All together, we compared the performance of 46 different model and variable selection combinations in addition to the benchmark model.

5.3 Results

Table 5-2 shows the variables selected by each method including interaction effects. The following variables were selected by all five variable selection methods: diabetes, functional status at registration, UNOS region, and the year placed on the waiting list.

Table 5-2: Variables selected by each of the variable selection methods. In the table, X:Y indicates an interaction between the variables X and Y.

Lasso	Permutation importance top 10	MARS	Permutation importance with interactions	MARS with interactions
DIAB	BMI_TCR	DIAB	BMI_TCR	FUNC_STAT_TCR_TEN
FUNC_STAT_TCR_TEN	DIAB	FUNC_STAT_TCR_TEN	DIAB	FUNC_STAT_TCR_TEN:REGION
INIT_AGE	DIALYSIS_DAYS_TO_WAITLIST	REGION	DIALYSIS_DAYS_TO_WAITLIST	FUNC_STAT_TCR_TEN:TOT_SERUM_ALBUM
REGION	FUNC_STAT_TCR_TEN	TOT_SERUM_ALBUM	FUNC_STAT_TCR_TEN	FUNC_STAT_TCR_TEN:WAITLIST_YEAR
TOT_SERUM_ALBUM	HGT_CM_TCR	WAITLIST_YEAR	HGT_CM_TCR	TOT_SERUM_ALBUM:REGION
WAITLIST_YEAR	INIT_AGE		INIT_AGE	WAITLIST_YEAR
	ON_DIALYSIS		ON_DIALYSIS	WAITLIST_YEAR:DIAB
	PROJECTED_PAYMENTSOURCE_AT_REGISTRATION		ON_DIALYSIS:FUNC_STAT_TCR_TEN	WAITLIST_YEAR:REGION
	REGION		ON_DIALYSIS:WAITLIST_YEAR	
	WAITLIST_YEAR		PROJECTED_PAYMENTSOURCE_AT_REGISTRATION	
			REGION	
			REGION:WAITLIST_YEAR	
			TOT_SERUM_ALBUM:FUNC_STAT_TCR_TEN	

Table 5-2 continued

Lasso	Permutation importance top 10	MARS	Permutation importance with interactions	MARS with interactions
			WAITLIST_YEAR	
			WAITLIST_YEAR:FUNC_STAT_TCR_TEN	

Figure 5-4 shows the top 10 ranked variables by PIRF and their respective permutation importance measures. Functional status at registration had the highest permutation importance and was ranked as the most-important predictive variable by PIRF. This result is consistent with the fact that 66% of the observations had the same functional status at transplantation as the functional status at registration. The next three most-important variables by permutation importance were the year placed on the waitlist, the age of the patient, and the number of days the patient had been on dialysis prior to waitlist registration.

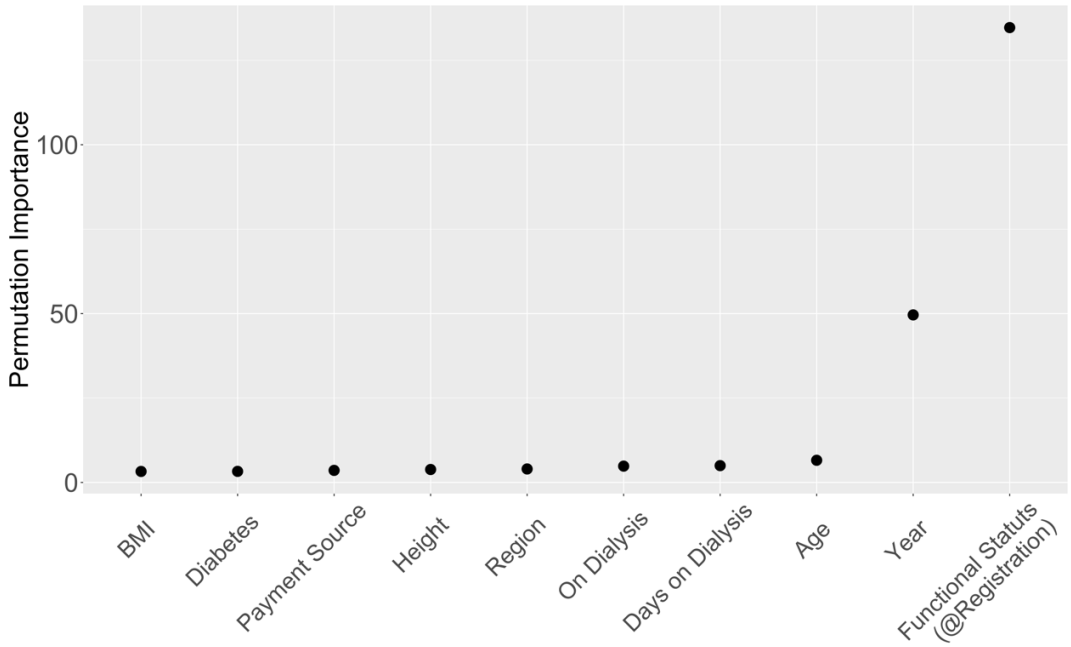

Figure 5-4: Top ten variables ranked by permutation importance using random forests.

Table 5-3 shows the RMSE, MSE, standard deviation of MSE, and accuracy of classification within one and two increments for each model and variable selection method combination.

Table 5-3: Performance of predictive models from cross-validation.

Model/variable Set Name	RMSE	MSE	σ MSE	Accuracy of classification within one increment	Accuracy of classification within two increments
Permutation importance interactions:	13.03	169.78	1.33	81.39%	92.61%

Table 5-3 continued

Model/variable Set Name	RMSE	MSE	σ MSE	Accuracy of classification within one increment	Accuracy of classification within two increments
generalized additive model					
Permutation importance interactions: generalized additive model without "ON_DIALYSIS"	13.05	170.18	1.08	81.33%	92.62%
Permutation importance top 10: generalized additive model	13.12	172.01	1.4	81.83%	92.05%
Lasso: generalized additive model	13.16	173.19	1.56	81.84%	91.99%
Permutation importance top 10: random forests	13.21	174.49	1.64	81.98%	92.16%
Permutation importance top 10: stacking using linear regression	13.21	174.55	1.55	82.18%	92.06%
Permutation importance top 10: neural networks	13.22	174.7	1.6	81.94%	91.77%
Permutation importance top 10: gradient boosting	13.22	174.73	1.6	82.19%	92.05%
MARS: generalized additive model	13.23	175.09	1.49	81.87%	91.75%
Permutation importance top 10: support vector machines	13.28	176.42	1.32	81.84%	91.66%
MARS interactions: generalized additive model	13.33	177.81	3.05	80.19%	92.64%
Permutation importance interactions: neural networks	13.37	178.66	2.12	81.5%	91.72%

Table 5-3 continued

Model/variable Set Name	RMSE	MSE	σ MSE	Accuracy of classification within one increment	Accuracy of classification within two increments
Permutation importance interactions: Box-Cox linear regression	13.45	181.01	1.37	81.09%	92.07%
Permutation importance interactions: linear regression	13.5	182.29	1.4	82.39%	91%
Permutation importance top 10: Box-Cox linear regression	13.53	183.18	1.65	80.85%	92.15%
Lasso: support vector machines	13.54	183.39	5.89	80.87%	91.77%
Permutation importance interactions: gradient boosting	13.55	183.63	4.73	80.98%	91.48%
Lasso: Box-Cox linear regression	13.56	183.88	1.59	81.06%	92.01%
MARS interactions: Box-Cox linear regression	13.56	183.98	1.7	81.51%	91.71%
Permutation importance interactions: random forests	13.57	184.25	5.2	80.47%	91.68%
Permutation importance top 10: linear regression	13.58	184.42	1.41	82.85%	90.78%
MARS: Box-Cox linear regression	13.58	184.44	1.6	80.89%	92%
Lasso: linear regression	13.6	184.94	1.34	83.04%	90.67%
Permutation importance interactions: stacking using linear regression	13.61	185.25	5.1	80.89%	91.39%
MARS interactions: linear regression	13.62	185.46	1.59	82.33%	91.1%

Table 5-3 continued

Model/variable Set Name	RMSE	MSE	σ MSE	Accuracy of classification within one increment	Accuracy of classification within two increments
MARS: linear regression	13.63	185.78	1.46	82.91%	90.61%
Lasso: neural networks	13.71	187.86	4.41	80.17%	91.32%
MARS interactions: neural networks	13.89	192.96	9.24	79.73%	90.99%
MARS: neural networks	13.9	193.18	6.16	79.72%	91.06%
MARS: support vector machines	14.47	209.43	10.16	79.42%	90.17%
Lasso: gradient boosting	14.51	210.73	11.36	79.07%	89.75%
Permutation importance top 10: gradient boosting (classification)	14.66	214.95	2.07	81.75%	88.82%
Functional status same as registration	14.68	215.57	2.01	80.55%	88.69%
Lasso: stacking using linear regression	14.7	216.17	13.98	78.85%	89.5%
Lasso: random forests	15.05	226.65	11.53	77.11%	88.61%
Permutation importance interactions: gradient boosting (classification)	15.44	238.56	9.04	80.12%	87.37%
MARS interactions: random forests	15.55	242.1	15.17	73.9%	88.04%
Permutation importance interactions: support vector machines	15.89	252.49	2.52	76.5%	87.54%
MARS interactions: stacking using linear regression	15.96	254.95	14.6	73.61%	87.59%
MARS: random forests	16.03	257.03	15.35	72.75%	86.76%
MARS interactions: gradient boosting	16.06	258.27	19.68	73.55%	87.17%
MARS interactions: support vector machines	16.22	263.23	2.08	77.62%	86.23%

Table 5-3 continued

Model/variable Set Name	RMSE	MSE	σ MSE	Accuracy of classification within one increment	Accuracy of classification within two increments
MARS: stacking using linear regression	16.24	264.97	38.62	72.42%	87.17%
MARS: gradient boosting	16.34	267.58	30.36	71.74%	86.98%
Lasso: gradient boosting (classification)	16.43	270.15	20.24	78.04%	85.47%
MARS interactions: gradient boosting (classification)	17.39	302.8	19.27	75.8%	83.48%
MARS: gradient boosting (classification)	17.64	311.65	25.44	74.94%	82.93%

Our final predictive model, a generalized additive model with the variables PIRF interactions without using 'ON_DIALYSIS' (GA-PIRF), resulted in an average RMSE of 13.05 based on 20 cross-validation samples. GA-PIRF performed significantly better than the benchmark model with an RMSE of 14.68 (a two sided paired t-test with equal variances comparing the RMSE for each cross validation sample yielded a p-value less than $2.2*10^{-16}$). GA-PIRF obtained an accuracy of classification within one increment of 81.33% and accuracy within two increments of 92.62% (compared to 80.55% and 88.69%, respectively, for the benchmark model). Table D-4 shows that GA-PIRF performs better than the benchmark model for every cross-validation sample. Additional performance metrics including the average RMSEs for the patients whose functional status changed vs. stayed the same in the out-of-sample data are shown in Table 5-4. We provide example code to build and make predictions with GA-PIRF in Text D-1. Further, including the

variable, 'ON_DIALYSIS', did not make a statistically significant difference in model performance based on RMSE (a two sided paired t-test with equal variances comparing the RMSE for each cross validation sample between GA-PIRF and including 'ON_DIALYSIS' in GA-PIRF, yielded a p-value of 0.2993).

Table 5-4: Additional performance metrics for our final predictive model compared to the benchmark model. Metrics include: the average RMSEs for observations where the functional status increased vs. decreased in the out-of-sample data, the average RMSEs for observations where the functional status changed vs. stayed the same in the out-of-sample data, and the average difference between the predictions and the actual functional status values. The performance is based on 20 cross-validation samples of 80% training and 20% out-of-sample data.

Model	RMSE when status increased	RMSE when status decreased	RMSE when status changed	RMSE when status stayed the same	Difference between prediction and actual status
GA-PIRF	17.76	20.31	19.37	6.9	-0.4
Benchmark	24.1	23.96	24.02	0	-1.79

The worst-performing model based on RMSE was the gradient boosting model with the softmax objective implemented with the variables selected by MARS, resulting in an RMSE of 17.64, accuracy of classification within one increment of 74.94%, and accuracy within two increments of 82.93%. Table D-5 gives the performance results per model, averaged for all variable selection methods. Table D-6 depicts the performance results per variable selection method, averaged across all models. We further list, in Table D-7, the

average optimal tuning parameters found from the hyper-parameter grid searches for each model.

5.4 Discussion

We built models to predict the functional status of a patient at transplantation, given information only known at waitlist registration. The model can be used to predict how the functional status of a patient may change while on the waitlist, from registration to transplantation. The model performs significantly better, across multiple metrics, compared to a benchmark model which assumes that the functional status will remain the same between registration and transplantation.

Predicting changes in functional status could be helpful especially when a patient is offered a deceased donor organ, while assessing the tradeoffs between accepting the offer and having a transplant, versus remaining on the waitlist for a potentially better organ offer that may arrive in the future. Functional status at transplantation is an important predictor of kidney transplant survival (controlling for other variables) (50), and hence, the decision to remain on the waitlist needs to consider the possibility of a change in functional status while on the waitlist. Figure 5-5 visualizes how higher functional status at transplantation is associated with higher post-transplant survival using the Kaplan–Meier estimate (26) using the same data we used in our analysis. Predicting the functional status at a future date, e.g., the (estimated) time of transplantation, can also be informative in estimating potential healthcare costs and caregiving needs (102).

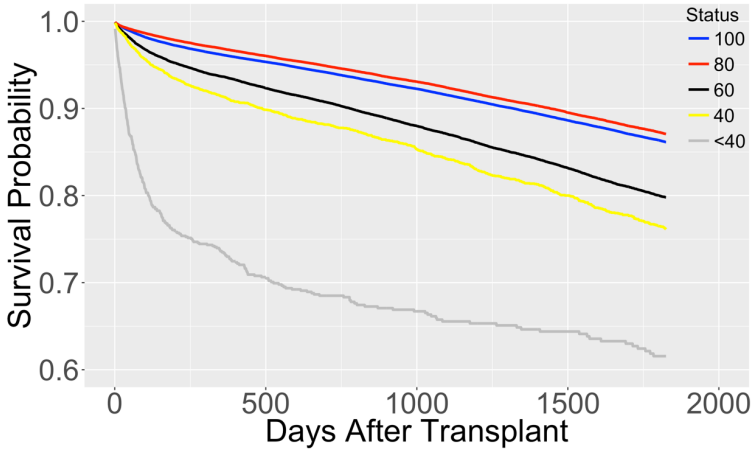

Figure 5-5: Post-transplant survival for different groups of patients based on their functional status at transplantation using the Kaplan–Meier estimate.

Our model focuses on predicting the functional status of a patient at a future date; it does not predict the likelihood of a patient dying while on the waitlist, nor does it predict the likelihood (and timing) of a patient to receive a transplant in the future. In our dataset, 17% of patients who were on the kidney waitlist were removed from the waitlist because they died or were too sick to receive a transplant. Models predicting the likelihood of transplantation (103) or death (46) before kidney transplantation, can be found in the literature, and be used in conjunction with the model proposed here, e.g., while evaluating decisions regarding organ offers.

A limitation of this analysis is that the KPS has been reported to have some subjectivity in its recording (104). A patient's true health status may be slightly different than their reported status. On the positive side, the usefulness of KPS in predicting post-transplant survival and the likelihood of receiving a kidney has been established in previous literature (6,83-87,105). Hence, even if there is some subjectivity in the recording of KPS

at registration, the high predictive accuracy of our model would still lead to useful information and insights for patients and physicians.

The proposed model utilizes data from UNOS. Additional data on a patient's lifestyle (e.g., nutrition, physical activity) can be incorporated into a more complex model for future research.

CHAPTER 6. ORGAN TRANSPLANT DECISION SUPPORT TOOL

Utilizing the transplant and waitlist survival models that we built in chapters 3 and 4, we created an interactive tool that can be used to show the survival curves of a patient either receiving an IRD organ or waiting for a non-IRD organ for the kidney, heart, liver and lung. The tool allows the user to enter and display the survival curves for custom characteristics of the recipient and the donor. The tool was built using the statistical software R version 3.3.2 (29) and key packages shiny (106) and ggplot2 (107). By default, the buttons on the tool are populated with the mean value for numerical variables and the most-common value for categorical variables, for the data used in each model scenario. In addition, a web and mobile version of the interactive tool is being built with the help of Georgia Tech Research Institute (108).

The following modification to the transplant and waitlist survival models for the kidney that we built in chapter 3 was made for the tool: we used the parameter, mincriterion = 0.75 instead of mincriterion = 0.25 (the value of the test statistic that must be exceeded in order to implement a split in the random survival forest algorithm), since it allowed us to grow forests that were less deep and build a model with faster loading and computation times with similar performance.

We also added an additional feature to the tool that shows the survival curve if the recipient receives a non-IRD organ immediately. For each organ, these models were trained on the same data that we used to train our models that predict the survival for a patient

receiving a non-IRD organ after waiting on the waitlist. However, we used variables known at transplantation in addition to information on the waiting list (for example, information about the donor is not known when the recipient decides to remain on the waitlist and receive a non-IRD organ in the future, but the donor information is known if the recipient is currently offered an non-IRD organ). For each organ, we built these transplant survival models using the same variables we used for the IRD transplant survival models. For the kidney, the transplant survival model was built using random survival forests with conditional inference trees as base learners (23,24), and the same hyper parameters we used for the transplant survival models in chapter 3 (25) except that we used the parameter mincriterion = 0.75 instead of the parameter mincriterion = 0.25. For the liver, heart and lung, the transplant survival models were built using the Cox proportional hazards model. Table 3-1 and Table 4-1 show the data used for building the models. Table 6-1 shows the performance of the predictive models used in the interactive tool based on ten cross-validation samples of 80% training data and 20% out-of-sample data.

Table 6-1: Performance of the predictive models used in the interactive tool based on ten cross-validation samples of 80% training data and 20% out-of-sample data.

Organ	Model	C index at 5 years	5 year integrated Brier score	Standard deviation of C index
Kidney	IRD	0.687	0.063	0.014
	Non-IRD (after waiting)	0.697	0.068	0.007
	Waitlist	0.685	0.102	0.005
	Non-IRD (immediately)	0.702	0.067	0.006
Heart	IRD	0.641	0.118	0.030
	Non-IRD (after waiting)	0.591	0.126	0.008

Table 6-1 continued

Organ	Model	C index at 5 years	5 year integrated Brier score	Standard deviation of C index
	Waitlist	0.749	0.161	0.006
	Non-IRD (immediately)	0.610	0.124	0.012
Liver	IRD	0.593	0.120	0.039
	Non-IRD (after waiting)	0.622	0.117	0.007
	Waitlist	0.804	0.142	0.005
	Non-IRD (immediately)	0.632	0.116	0.010
Lung	IRD	0.596	0.182	0.023
	Non-IRD (after waiting)	0.568	0.182	0.009
	Waitlist	0.788	0.158	0.010
	Non-IRD (immediately)	0.580	0.181	0.005

Figure 6-1, Figure 6-2, Figure 6-3, and Figure 6-4 show screenshots of the interactive tool for the kidney, heart, liver and lung respectively.

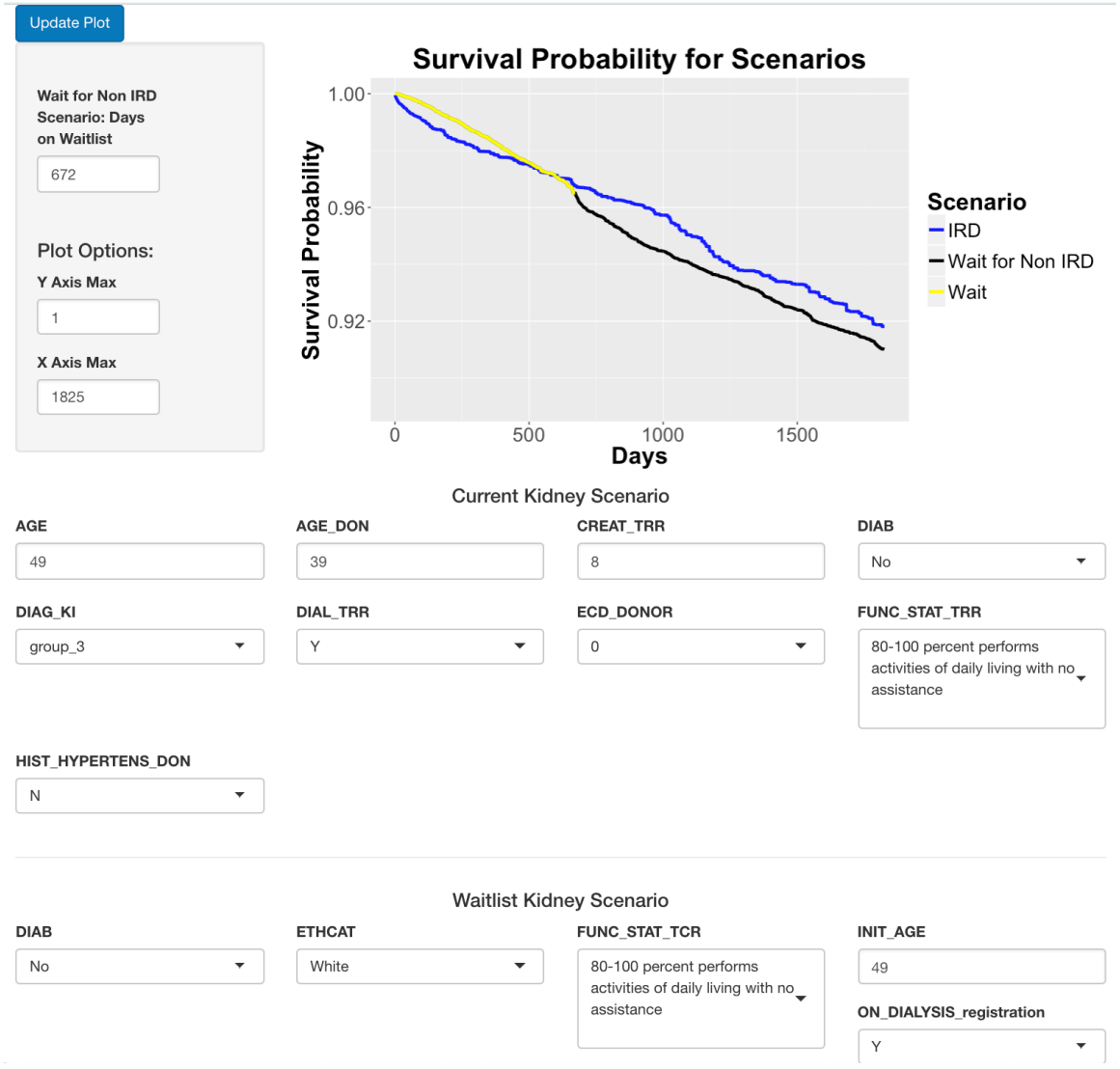

Figure 6-1: Screenshot of the interactive decision support tool for the kidney, populated with the default variable values.

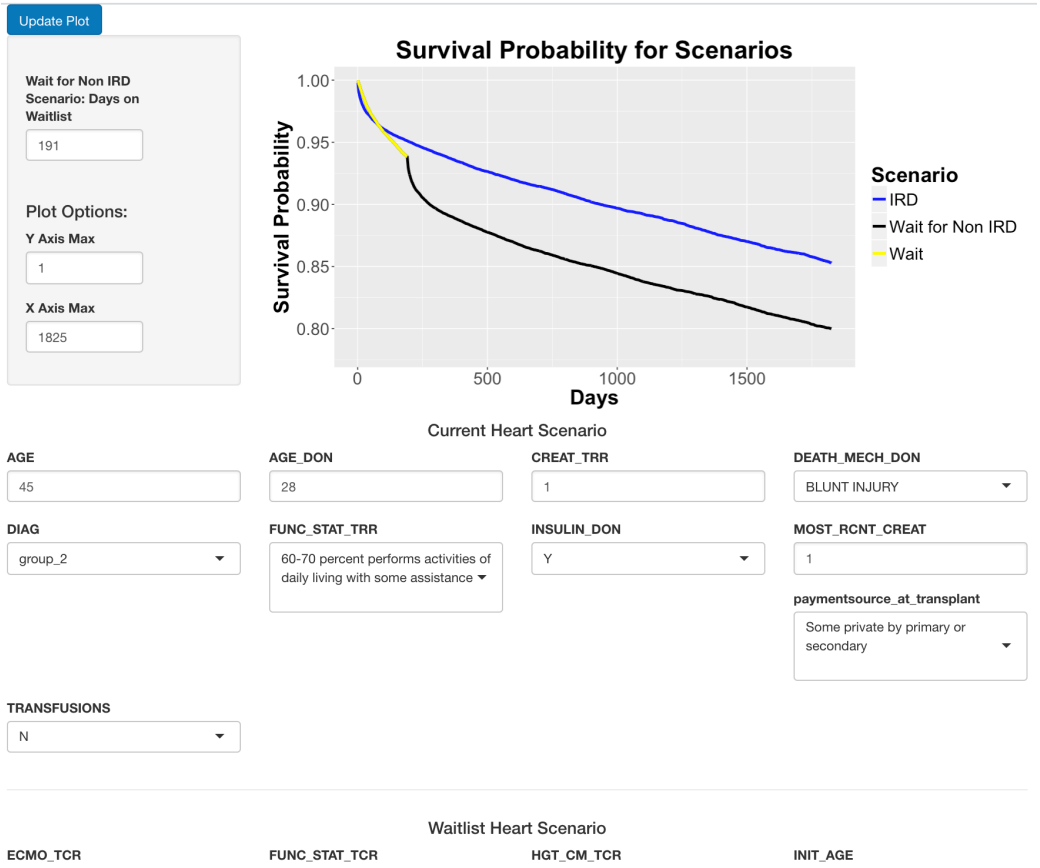

Figure 6-2: Screenshot of the interactive decision support tool for the heart, populated with the default variable values.

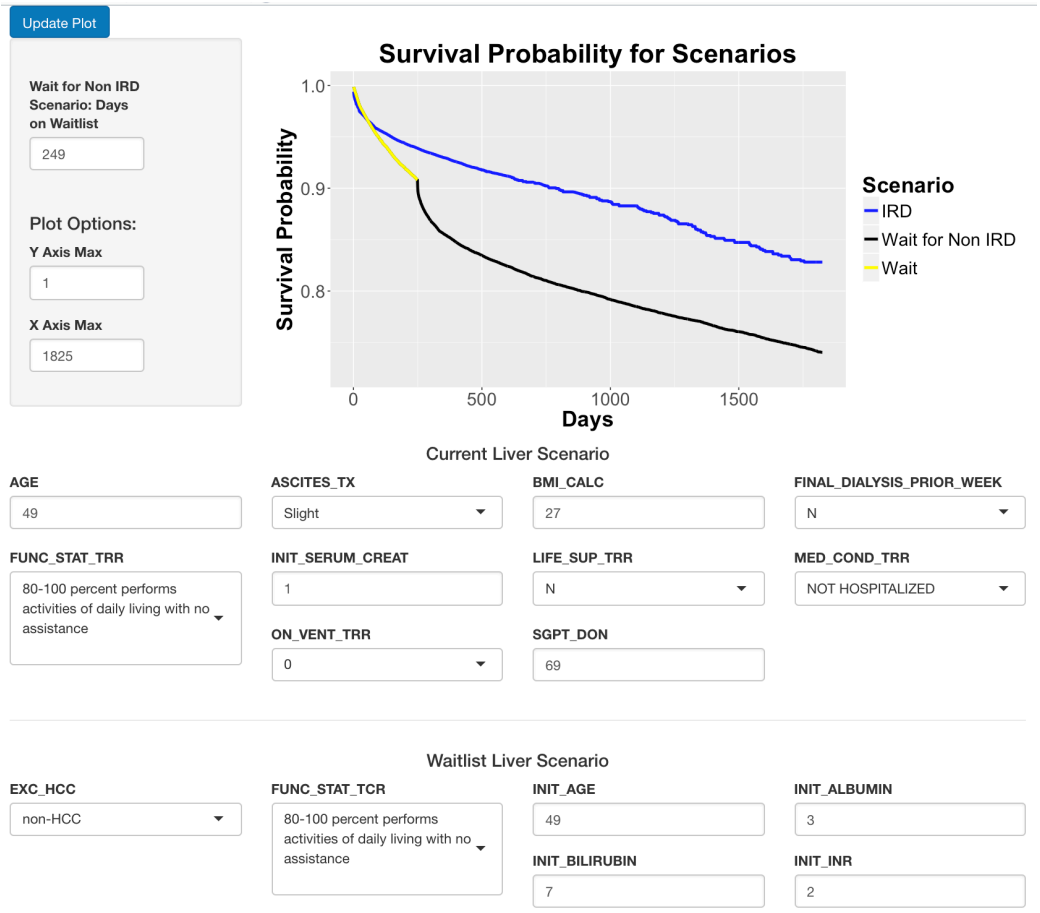

Figure 6-3: Screenshot of the interactive decision support tool for the liver, populated with the default variable values.

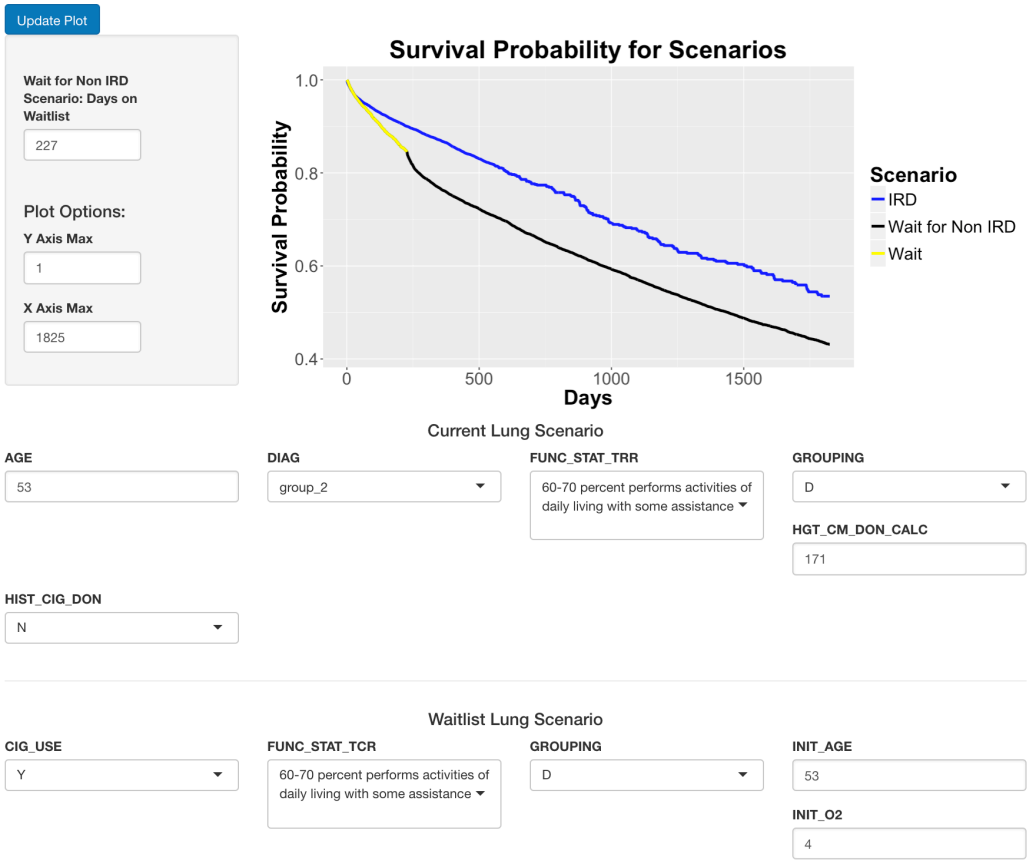

Figure 6-4: Screenshot of the interactive decision support tool for the lung, populated with the default variable values.

CHAPTER 7. CONCLUSION

We found that the simulations had, on average, higher 5-year survival probabilities receiving an IRD organ versus waiting for one day and receiving a non-IRD organ, for all four organs. As estimated wait times increased, the difference also increased, suggesting that patients who are likely to wait for longer times would benefit more from receiving an IRD organ (versus waiting and receiving a non-IRD organ later). In practice, given the high uncertainty about wait times, the majority of transplant recipients may have a higher survival probability receiving the IRD organ; in fact, it has been shown that among those patients who received an IRD offer and declined, only 31.0% received a non-IRD kidney within 5 years (43). Differences in the survival probabilities for receiving an IRD organ or waiting for a non-IRD organ for a particular set of donor and recipient characteristics can be calculated using our benefit equations or our interactive decision support tool.

Our transplant and waitlist survival models used training data prior to 2014. Hence, due to advancements in medical care in recent years, our survival estimates may be conservative. Figure 7-1 shows that transplant survival for kidney transplant recipients has improved over time (without controlling for other factors). For further research, it would be beneficial to see the benefit for IRD organs when we can obtain 5-year survival data that takes into account the latest treatments for infectious diseases. Another area for future research would be to explore the affects of seasonality on transplant and waitlist survival. Figure 7-2 shows how transplant survival was lower for patients receiving transplants on the weekend than during the week. It would be interesting to explore why this occurs and if the affect still holds when controlling for other factors.

Throughout this thesis, we built many predictive models. For example, when we predicted how the functional status of a kidney transplant patient changes from registration

to transplantation, we cross-validated many different predictive models and chose to use the model with the greatest performance. When building models to predict medical outcomes, it may also be important to make sure the models are explainable and interpretable. For further research it would be helpful to develop a framework for the tradeoffs between model interpretability vs. complexity and performance.

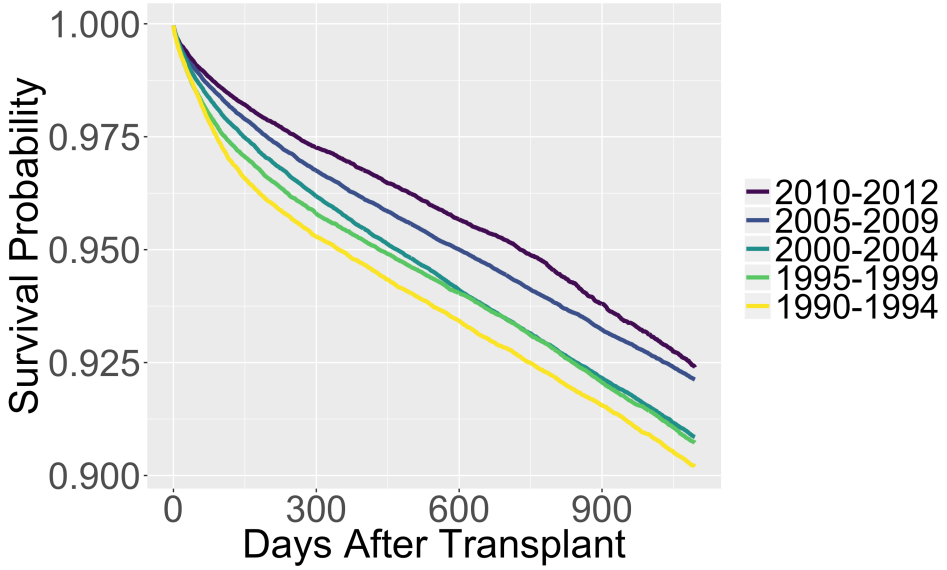

Figure 7-1: Transplant survival (using the Kaplan–Meier estimator) for kidney transplant recipients based on the year they received the transplant. The survival is based on all kidney transplant observations in our dataset with a recorded follow-up/death time and censored status (a total of 357,030 transplant observations from October 1 1987 to March 31 2014). The years listed in the legend are inclusive.

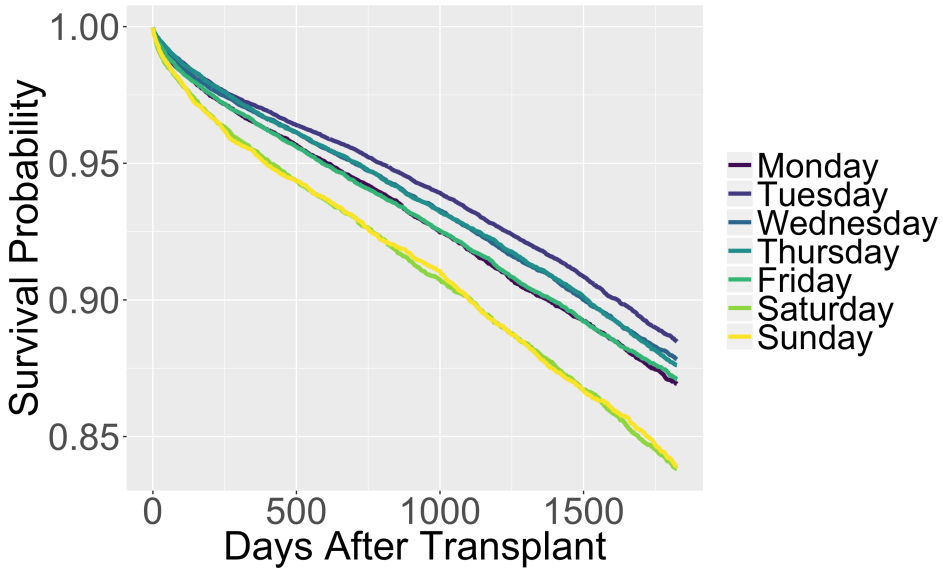

Figure 7-2: Transplant survival (using the Kaplan–Meier estimator) for kidney transplant recipients over the last 10 years in our data set, based on the day of the week that they received a transplant. The survival is based on all kidney transplant observations in our dataset with a recorded follow-up/death time and censored status between January 1 2004 and March 31 2014 inclusive (a total of 170,381 transplant observations).

One of the take-aways from this thesis is that there is potential to improve the survival prospects for patients on the organ transplant waitlist. Organs with the IRD label remain underutilized (44). For example, IRD kidneys were found to be one-third less likely to be used for transplantation than non-IRD kidneys with similar characteristics (38). Hence, helping patients decide whether to accept an IRD organ offer can increase utilization of organs, help them make the best choice that maximizes their survival and saves lives.

Further, our transplant survival model with increased performance over the current model in the kidney allocation system, may be utilized to improve the efficiency of the matching process and also increase the utilization rate for standard organs. In 2009 for example, 19.2% of deceased donor kidneys recovered for transplant were discarded, up from 5.1% in 1988 (40). Our model for how the functional status of a patient changes from

waitlist registration to transplantation, can also help in the allocation process by providing an estimate of the patient's health when they would receive a transplant. Using similar methods, predicting how the MELD score changes from waitlist registration to liver transplantation is also a great area for further research.

As the majority of the kidney discard rate rise can be explained by the broadening donor pool (40), the methods used to compare the survival of a patient accepting an IRD organ offer or waiting for a non-IRD organ can be extended to other types of non-standard donors, such as expanded criteria donors (ECD). The use of machine learning and statistical methods applied in the field of healthcare is promising and can save many lives.

APPENDIX A. APPENDIX FOR CHAPTER 2

Table A-1: Log-rank test for differences in cohort survival. χ^2 statistic value = 259.3, *p*-value = 0.

Cohort	Observed	Expected
1987–2001	47915	45945
2002–2014	25860	27830

Text A-1: Grouping values for the variable kidney diagnosis.

To group and reduce the number of possible values for the variable kidney diagnosis:

1. Use domain knowledge to initially assign related values into the same group.
2. Create binary variables (dummy variables) corresponding to each of the remaining values for the categorical variable.
3. Build a Cox proportional hazards model to predict recipient post-transplant survival using the binary variables from step 2, in addition to other relevant variables to control for, such as recipient age.
4. Sort the coefficients for the binary variables corresponding to the categorical variable from the Cox model into a prespecified number of quantiles, representing the new categorical variable values.

Table A-2: Original kidney diagnosis values and their new groupings. We used the coefficients of a Cox model to group values with similar predicted transplant survival, controlling for other variables. We controlled for: recipient age, recipient diabetes, recipient cold ischemia time, recipient initial waitlist status, recipient ethnicity, donor age,

donor cause of death, and donor living status. We considered putting the first three values of kidney diagnosis in its own group. However, they had fewer than 90 observations combined, which may cause overfitting issues.

Factor Level	Coefficient	New group
THIN BASEMENT MEMBRANE DISEASE	-12.018	1
HIV NEPHROPATHY	-11.659	1
DYSPLASIA	-10.185	1
GOUT	-1.655	1
MEDULLARY CYSTIC DISEASE	-1.042	1
GOODPASTURE'S SYNDROME	-0.771	1
LYMPHOMA	-0.732	1
ALPORT'S SYNDROME	-0.689	1
IGA NEPHROPATHY	-0.629	1
ANTI-GBM	-0.585	2
FAMILIAL NEPHROPATHY	-0.572	2
POLYCYSTIC KIDNEYS	-0.551	2
RHEUMATOID ARTHRITIS	-0.518	2
HENOCH-SCHOENLEIN PURPURA	-0.416	2
FOCAL GLOMERULAR SCLEROSIS (FOCAL SEGMENTAL - FSG)	-0.287	2
CHRONIC PYELONEPHRITIS/REFLUX NEPHROPATH	-0.217	2
UROLITHIASIS	-0.210	2
IDIO/POST-INF CRESCENTIC GLOMERULONEPHRI	-0.209	3
CONGENITAL OBSTRUCTIVE UROPATHY	-0.205	3
NEPHROLITHIASIS	-0.201	3
CHRONIC GLOMERULONEPHRITIS UNSPECIFIED	-0.196	3
MEMBRANOUS GLOMERULONEPHRITIS	-0.160	3
RAPID PROGRESSIVE GLOMERULONEPHRITIS (RPGN)	-0.094	3
WEGENERS GRANULOMATOSIS	-0.092	3
MALIGNANT HYPERTENSION	-0.077	3
MEMBRANOUS NEPHROPATHY	-0.060	3
CHRONIC NEPHROSCLEROSIS-UNSPECIFIED	-0.054	4

Table A-2 continued

Factor Level	Coefficient	New group
DRUG RELATED INTERSTITIAL NEPHRITIS	-0.022	4
CHRONIC GLOMERULOSCLEROSIS UNSPECIFIED	-0.019	4
NEPHRITIS	-0.009	4
ACQUIRED OBSTRUCTIVE NEPHROPATHY	0.000	4
OXALATE NEPHROPATHY (INCLUDES HEREDITARY OXALOSIS)	0.025	4
HYPERTENSIVE NEPHROSCLEROSIS	0.038	4
SYSTEMIC LUPUS ERYTHEMATOSUS	0.041	4
RENAL CELL CARCINOMA	0.062	5
NEPHROPHTHISIS	0.064	5
MESANGIO-CAPILLARY 1 GLOMERULONEPHRITIS	0.121	5
CHOLESTEROL EMBOLIZATION	0.125	5
POLYARTERITIS	0.137	5
OTHER SPECIFY	0.141	5
RENAL ARTERY THROMBOSIS	0.142	5
ANTIBIOTIC-INDUCED NEPHRITIS	0.152	5
SARCOIDOSIS	0.153	6
HYPOPLASIA/DYSPLASIA/DYSGENSIS/AGE NESIS	0.166	6
HEROIN NEPHROTOXICITY	0.181	6
DIABETES	0.182	6
ANALGESIC NEPHROPATHY	0.194	6
INCIDENTAL CARCINOMA	0.203	6
HEMOLYTIC UREMIC SYNDROME	0.211	6
RETRANSPLANT/GRAFT FAILURE	0.218	6
PROGRESSIVE SYSTEMIC SCLEROSIS	0.252	6
PRUNE BELLY SYNDROME	0.314	7
ACUTE TUBULAR NECROSIS	0.373	7
FABRY'S DISEASE	0.384	7
CANCER CHEMOTHERAPY INDUCED NEPHRITIS	0.424	7
MYELOMA	0.446	7
WILMS' TUMOR	0.479	7

Table A-2 continued

Factor Level	Coefficient	New group
CORTICAL NECROSIS	0.486	7
MESANGIO-CAPILLARY 2 GLOMERULONEPHRITIS	0.491	7
LITHIUM TOXICITY	0.506	8
AMYLOIDOSIS	0.595	8
SCLERODERMA	0.611	8
CALCINEURIN INHIBITOR NEPHROTOXICITY	0.617	8
CYSTINOSIS	0.685	8
RADIATION NEPHRITIS	0.740	8
PRE-BMTRANSPLANTATION TOTAL BODY IRRADIATION	0.748	8
HEPATORENAL SYNDROME	0.765	8
SICKLE CELL ANEMIA	1.034	8

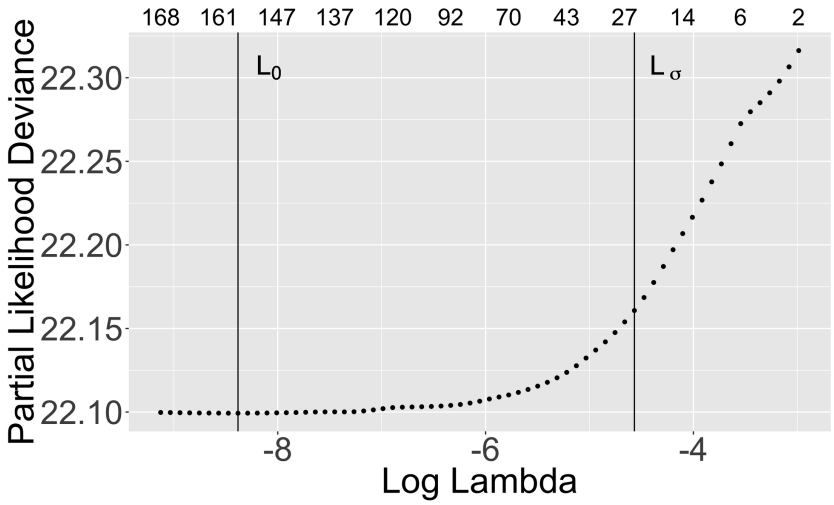

Figure A-1: Lasso variable selection for recipients ages 51 and older.

Table A-3: Descriptions of variables used in the proposed model. *See Table A-2 for variable values in this group.

Variable name	Description	Categories
AGE	Recipient age (yrs)	NA
AGE_DON	Donor age (yrs)	NA
ANY_DIAL	Recipient on dialysis any time between registration and transplant	NO, NOT_KNOWN, YES
COD_CAD_DON	Deceased donor-cause of death	ANOXIA, CEREBROVASCULAR/STROKE, CNS TUMOR, HEAD TRAUMA, NOT_KNOWN, OTHER SPECIFY
COLD_ISCH_KI	Kidney cold ischemic time (hours)	NA
CREAT_TRR	Recipient serum creatinine at time of transplant	NA
DEATH_MECH_DON	Deceased donor-mechanism of death	ASPHYXIATION, BLUNT INJURY, CARDIOVASCULAR, DEATH FROM NATURAL CAUSES, DROWNING, DRUG INTOXICATION, ELECTRICAL, INTRACRANIAL HEMORRHAGE/STROKE, NONE OF THE ABOVE, NOT_KNOWN, SEIZURE, SIDS, STAB OR GUNSHOT WOUND
DIAB	Recipient diabetes at registration	NO, NOT_KNOWN, YES
DIAG_KI	Kidney recipient primary diagnosis at transplant	GROUP_1*, GROUP_2*, GROUP_3*, GROUP_4*, GROUP_5*, GROUP_6*, GROUP_7*, GROUP_8*, NOT_KNOWN
DRUGTRT_COPD	Recipient drug treated COPD at registration	NO, NOT_KNOWN, YES
ETHCAT	Recipient ethnicity category	AMER IND/ALASKA NATIVE, ASIAN, BLACK, HISPANIC,

Table A-3 continued

Variable name	Description	Categories
		MULTIRACIAL, NATIVE HAWAIIAN/OTHER PACIFIC ISLANDER, NOT_KNOWN, WHITE
FUNC_STAT_TRR	Recipient functional status at transplant	10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY, 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT, 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE, 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE, NOT APPLICABLE (PATIENT < 1 YEAR OLD), NOT_KNOWN, PERFORMS ACTIVITIES OF DAILY LIVING WITH TOTAL ASSISTANCE.
HCV_SEROSTATUS	Recipient HCV status	NEGATIVE, NOT DONE, NOT_KNOWN, POSITIVE
HIST_DIABETES_DON	Deceased donor-history of diabetes, including duration of disease	NO, NOT_KNOWN, YES
HIST_HYPERTENS_DON	Deceased donor-history of hypertension	NO, NOT_KNOWN, YES
MED_COND_TRR	Recipient medical condition pre-transplant at transplant	HOSPITALIZED NOT IN ICU, IN INTENSIVE CARE UNIT, NOT HOSPITALIZED
PAYMENTSOURCE_AT_TRANSPLANT	Recipient primary payment source	CHIP, DONATION OR FREE CARE, MEDICAID, MEDICARE, NOT_KNOWN, OTHER, OTHER GOVERNMENT OR DEPARTMENT OF VA, SELF, SOME PRIVATE BY PRIMARY OR SECONDARY
REGION	UNOS region where transplanted	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

Table A-4: Summary of variables used in the predictive models. The mean value of the data is given for numeric variables and the percentage of observations for each category is given for categorical variables. *See Table A-2 for variable values in this group.

Variable	Variable Summary
AGE	48.5
AGE_DON	38.7
ANY_DIAL: N	6%
ANY_DIAL: NOT KNOWN	11.3%
ANY_DIAL: Y	82.6%
COD_CAD_DON: ANOXIA	12.9%
COD_CAD_DON: CEREBROVASCULAR/STROKE	24.8%
COD_CAD_DON: CNS TUMOR	0.4%
COD_CAD_DON: HEAD TRAUMA	28.1%
COD_CAD_DON: NOT KNOWN	32.3%
COD_CAD_DON: OTHER SPECIFY	1.6%
COLD_ISCH_KI	12.8
CREAT_TRR	7.8
DEATH_MECH_DON: ASPHYXIATION	2.1%
DEATH_MECH_DON: BLUNT INJURY	19.1%
DEATH_MECH_DON: CARDIOVASCULAR	6.5%
DEATH_MECH_DON: DEATH FROM NATURAL CAUSES	1.1%
DEATH_MECH_DON: DROWNING	0.6%
DEATH_MECH_DON: DRUG INTOXICATION	2.4%
DEATH_MECH_DON: ELECTRICAL	<0.1%
DEATH_MECH_DON: INTRACRANIAL HEMORRHAGE/STROKE	25.9%
DEATH_MECH_DON: NONE OF THE ABOVE	2%
DEATH_MECH_DON: NOT KNOWN	32.3%
DEATH_MECH_DON: SEIZURE	0.6%
DEATH_MECH_DON: SIDS	<0.1%
DEATH_MECH_DON: STAB OR GUNSHOT WOUND	7.3%
DIAB: NO	68.5%
DIAB: NOT KNOWN	1.5%
DIAB: YES	30%

Table A-4 continued

Variable	Variable Summary
DIAG_KI: GROUP_1*	5.6%
DIAG_KI: GROUP_2*	16.9%
DIAG_KI: GROUP_3*	10.5%
DIAG_KI: GROUP_4*	25.3%
DIAG_KI: GROUP_5*	7.3%
DIAG_KI: GROUP_6*	31.6%
DIAG_KI: GROUP_7*	0.7%
DIAG_KI: GROUP_8*	1.5%
DIAG_KI: NOT KNOWN	0.7%
DRUGTRT_COPD: N	94.7%
DRUGTRT_COPD: NOT KNOWN	4.3%
DRUGTRT_COPD: Y	1%
ETHCAT: AMER IND/ALASKA NATIVE	0.9%
ETHCAT: ASIAN	5%
ETHCAT: BLACK	25.6%
ETHCAT: HISPANIC	14%
ETHCAT: MULTIRACIAL	0.6%
ETHCAT: NATIVE HAWAIIAN/OTHER PACIFIC ISLANDER	0.4%
ETHCAT: NOT KNOWN	<0.1%
ETHCAT: WHITE	53.5%
FUNC_STAT_TRR: 10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY	0.5%
FUNC_STAT_TRR: 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT	2.7%
FUNC_STAT_TRR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE	17.7%
FUNC_STAT_TRR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE	73.3%
FUNC_STAT_TRR: NOT APPLICABLE (PATIENT < 1 YEAR OLD)	0.5%
FUNC_STAT_TRR: NOT KNOWN	5.2%
FUNC_STAT_TRR: PERFORMS ACTIVITIES OF DAILY LIVING WITH TOTAL ASSISTANCE.	0.1%

Table A-4 continued

Variable	Variable Summary
HCV_SEROSTATUS: NEGATIVE	87.6%
HCV_SEROSTATUS: NOT DONE	4.2%
HCV_SEROSTATUS: NOT KNOWN	3.2%
HCV_SEROSTATUS: POSITIVE	5.1%
HIST_DIABETES_DON: NO	63.2%
HIST_DIABETES_DON: NOT KNOWN	32.6%
HIST_DIABETES_DON: YES	4.2%
HIST_HYPERTENS_DON: N	75.4%
HIST_HYPERTENS_DON: NOT KNOWN	7%
HIST_HYPERTENS_DON: Y	17.7%
MED_COND_TRR: HOSPITALIZED NOT IN ICU	1.7%
MED_COND_TRR: IN INTENSIVE CARE UNIT	0.6%
MED_COND_TRR: NOT HOSPITALIZED	97.8%
PAYMENTSOURCE_AT_TRANSPLANT: CHIP	0.2%
PAYMENTSOURCE_AT_TRANSPLANT: DONATION OR FREE CARE	0.1%
PAYMENTSOURCE_AT_TRANSPLANT: MEDICAID	5.4%
PAYMENTSOURCE_AT_TRANSPLANT: MEDICARE	44.5%
PAYMENTSOURCE_AT_TRANSPLANT: NOT KNOWN	<0.1%
PAYMENTSOURCE_AT_TRANSPLANT: OTHER	0.1%
PAYMENTSOURCE_AT_TRANSPLANT: OTHER GOVERNMENT OR DEPARTMENT OF VA	1.4%
PAYMENTSOURCE_AT_TRANSPLANT: SELF	0.2%
PAYMENTSOURCE_AT_TRANSPLANT: SOME PRIVATE BY PRIMARY OR SECONDARY	48.2%
REGION: 1	3.1%
REGION: 10	9.3%
REGION: 11	9.6%
REGION: 2	14.1%
REGION: 3	12.6%
REGION: 4	8.2%
REGION: 5	15.8%

Table A-4 continued

Variable	Variable Summary
REGION: 6	3.8%
REGION: 7	9.7%
REGION: 8	6.9%
REGION: 9	7%

Table A-5: Cox proportional hazards model coefficients for the proposed model. Trained on a random sample of 100,000 observations.

Variable Name	Coefficient	*p*-Value
AGE	0.05	0
AGE_DON	0.01	0
ANY_DIAL: Base Level - NO		
ANY_DIAL: NOT_KNOWN	-0.05	0.37
ANY_DIAL: YES	0.45	0
COD_CAD_DON: Base Level - ANOXIA		
COD_CAD_DON: CEREBROVASCULAR STROKE	-0.08	0.21
COD_CAD_DON: CNS TUMOR	-0.21	0.15
COD_CAD_DON: HEAD TRAUMA	-0.01	0.85
COD_CAD_DON: NOT_KNOWN	-0.35	0
COD_CAD_DON: OTHER SPECIFY	-0.13	0.12
COLD_ISCH_KI	0	0
CREAT_TRR	-0.03	0
DEATH_MECH_DON: Base Level - ASPHYXIATION		
DEATH_MECH_DON: BLUNT INJURY	0	0.98
DEATH_MECH_DON: CARDIOVASCULAR	0.07	0.38
DEATH_MECH_DON: DEATH FROM NATURAL CAUSES	0.3	0.01
DEATH_MECH_DON: DROWNING	0.09	0.55
DEATH_MECH_DON: DRUG INTOXICATION	-0.02	0.8
DEATH_MECH_DON: ELECTRICAL	-0.98	0.17

Table A-5 continued

Variable Name	Coefficient	*p*-Value
DEATH_MECH_DON: INTRACRANIAL HEMORRHAGE STROKE	0.16	0.11
DEATH_MECH_DON: NONE OF THE ABOVE	0.16	0.12
DEATH_MECH_DON: SEIZURE	0.22	0.12
DEATH_MECH_DON: SIDS	-0.64	0.52
DEATH_MECH_DON: STAB OR GUNSHOT WOUND	-0.01	0.9
DIAB: Base Level - NO		
DIAB: NOT_KNOWN	-0.01	0.88
DIAB: YES	0.28	0
DIAG_KI: Base Level - GROUP_1		
DIAG_KI: GROUP_2	0.28	0
DIAG_KI: GROUP_3	0.5	0
DIAG_KI: GROUP_4	0.7	0
DIAG_KI: GROUP_5	0.69	0
DIAG_KI: GROUP_6	0.79	0
DIAG_KI: GROUP_7	0.79	0
DIAG_KI: GROUP_8	1.05	0
DIAG_KI: NOT_KNOWN	0.61	0
DRUGTRT_COPD: Base Level - NO		
DRUGTRT_COPD: NOT_KNOWN	0.04	0.42
DRUGTRT_COPD: YES	0.33	0
ETHCAT: Base Level - AMER IND/ALASKA NATIVE		
ETHCAT: ASIAN	-0.29	0
ETHCAT: BLACK	-0.01	0.93
ETHCAT: HISPANIC	-0.18	0.06
ETHCAT: MULTIRACIAL	0.17	0.28
ETHCAT: NATIVE HAWAIIAN OTHER PACIFIC ISLANDER	-0.02	0.92
ETHCAT: NOT_KNOWN	3.58	0
ETHCAT: WHITE	0.14	0.12
FUNC_STAT_TRR: Base Level - 10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY		

Table A-5 continued

Variable Name	Coefficient	*p*-Value
FUNC_STAT_TRR: 30 50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT	-0.6	0
FUNC_STAT_TRR: 60 70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE	-0.81	0
FUNC_STAT_TRR: 80 100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE	-1.03	0
FUNC_STAT_TRR: NOT APPLICABLE PATIENT 1 YEAR OLD	-0.56	0
FUNC_STAT_TRR: NOT_KNOWN	-0.94	0
FUNC_STAT_TRR: PERFORMS ACTIVITIES OF DAILY LIVING WITH TOTAL ASSISTANCE	-0.63	0.06
HCV_SEROSTATUS: Base Level - NEGATIVE		
HCV_SEROSTATUS: NOT DONE	0.03	0.47
HCV_SEROSTATUS: NOT_KNOWN	0.07	0.13
HCV_SEROSTATUS: POSITIVE	0.52	0
HIST_HYPERTENS_DON: Base Level - NO		
HIST_HYPERTENS_DON: NOT_KNOWN	0.22	0
HIST_HYPERTENS_DON: YES	0.1	0

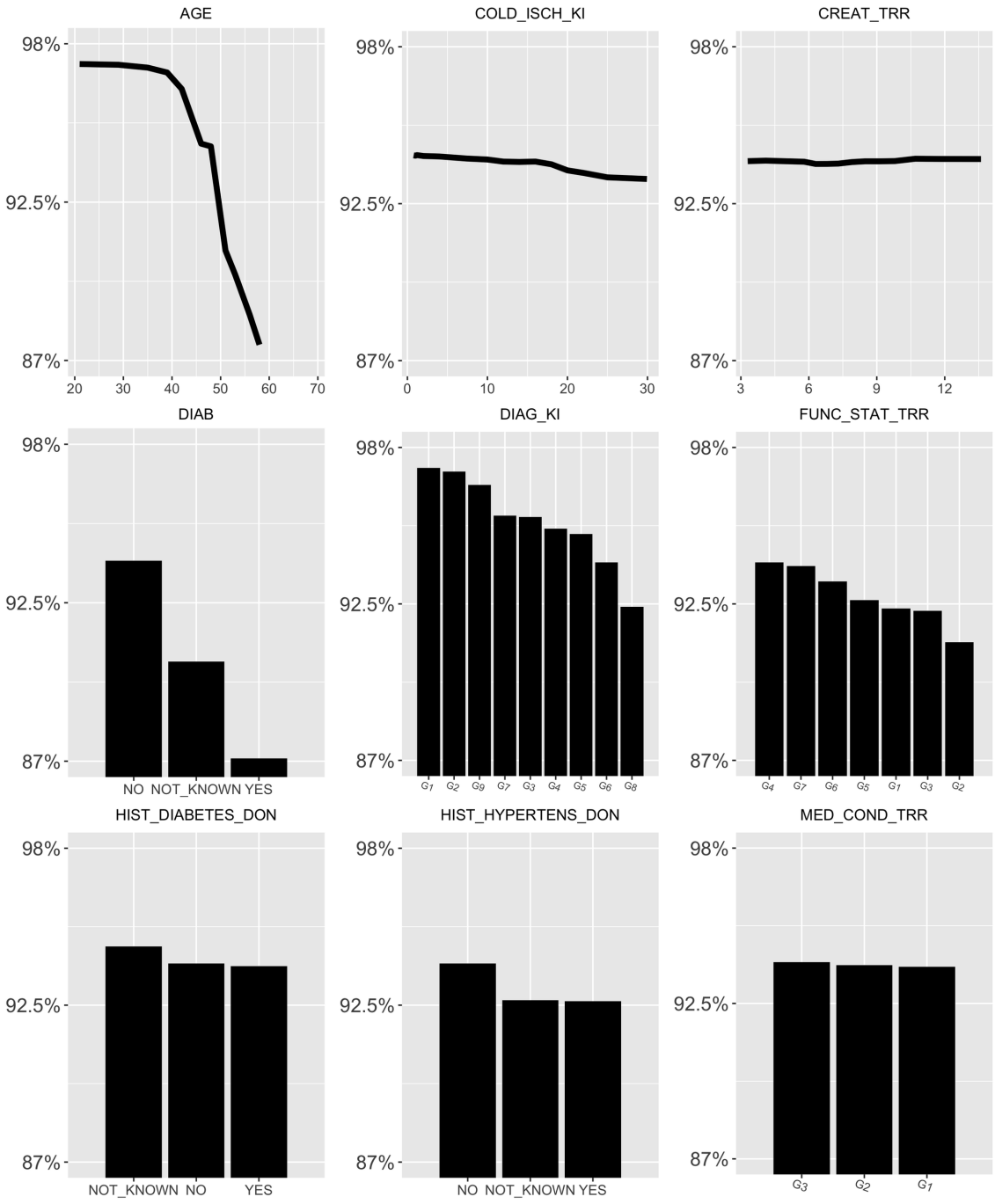

Figure A-2: Proposed model's 5-year survival predictions for different variable values. In each plot, variable values not shown are held constant and listed in Table A-6. The model was trained on 100,000 random training observations.

Table A-6: Variables held constant in Figure A-2. *See Table A-2 for variable values in this group.

Constant features	Value
AGE	48.5
AGE_DON	38.7
ANY_DIAL	Y
COD_CAD_DON	NOT_KNOWN
COLD_ISCH_KI	12.8
CREAT_TRR	7.8
DEATH_MECH_DON	NOT_KNOWN
DIAB	NO
DIAG_KI	GROUP_6*
DRUGTRT_COPD	N
ETHCAT	WHITE
FUNC_STAT_TRR	80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE
HCV_SEROSTATUS	NEGATIVE
HIST_DIABETES_DON	NO
HIST_HYPERTENS_DON	N
MED_COND_TRR	NOT HOSPITALIZED
PAYMENTSOURCE_AT_TRANSPLANT	SOME PRIVATE BY PRIMARY OR SECONDARY
REGION	5

Table A-7: Factor level legend for Figure A-2.

Factor level name	Description
DIAG_KI G1	GROUP_1*
DIAG_KI G2	GROUP_2*
DIAG_KI G3	GROUP_3*
DIAG_KI G4	GROUP_4*

Table A-7 continued

Factor level name	Description
DIAG_KI G5	GROUP_5*
DIAG_KI G6	GROUP_6*
DIAG_KI G7	GROUP_7*
DIAG_KI G8	GROUP_8*
DIAG_KI G9	NOT_KNOWN
FUNC_STAT_TRR G1	10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY
FUNC_STAT_TRR G2	30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT
FUNC_STAT_TRR G3	60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE
FUNC_STAT_TRR G4	80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE
FUNC_STAT_TRR G5	NOT APPLICABLE (PATIENT < 1 YEAR OLD)
FUNC_STAT_TRR G6	NOT_KNOWN
FUNC_STAT_TRR G7	PERFORMS ACTIVITIES OF DAILY LIVING WITH TOTAL ASSISTANCE.
MED_COND_TRR G1	HOSPITALIZED NOT IN ICU
MED_COND_TRR G2	IN INTENSIVE CARE UNIT
MED_COND_TRR G3	NOT HOSPITALIZED

Table A-8: Concordance index at different days after transplant for the proposed model. The performance is calculated from 10 random samples of 80,000 training observations and 20,000 out-of-sample observations.

Days	C-index
10	0.720
50	0.722
100	0.723
250	0.724
500	0.724
1000	0.724
1500	0.724
2000	0.724

Table A-9: Proposed model performance by category. Performance from a random sample of 100,000 training observations and 25,000 out-of-sample observations.

Group	5-Year integrated Brier score	C-index
AGE_DON: 0 - 24	0.051	0.730
AGE_DON: 24 - 35	0.044	0.742
AGE_DON: 35 - 44	0.057	0.717
AGE_DON: 44 - 53	0.064	0.710
AGE_DON: 53 - 84	0.090	0.688
AGE: 0 - 36	0.023	0.670
AGE: 36 - 47	0.038	0.702
AGE: 47 - 55	0.061	0.652
AGE: 55 - 62	0.079	0.640
AGE: 62 - 90	0.109	0.637
COLD_ISCH_KI: 0.01 - 1.4	0.037	0.732
COLD_ISCH_KI: 1.4 - 8.4	0.053	0.731
COLD_ISCH_KI: 8.4 - 15	0.070	0.707
COLD_ISCH_KI: 15 - 22	0.073	0.703
COLD_ISCH_KI: 22 - 99	0.077	0.703
DIAB: NO	0.046	0.727
DIAB: YES	0.095	0.650
FUNC_STAT_TRR: 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT	0.103	0.704
FUNC_STAT_TRR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE	0.078	0.686
FUNC_STAT_TRR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE	0.055	0.730
FUNC_STAT_TRR: NOT_KNOWN	0.064	0.714
HIST_DIABETES_DON: NO	0.070	0.706
HIST_DIABETES_DON: NOT_KNOWN	0.039	0.732

Table A-9 continued

Group	5-Year integrated Brier score	C-index
HIST_DIABETES_DON: YES	0.108	0.682
HIST_HYPERTENS_DON: NO	0.055	0.728
HIST_HYPERTENS_DON: NOT_KNOWN	0.052	0.736
HIST_HYPERTENS_DON: YES	0.091	0.674
PAYMENTSOURCE_AT_TRANSPLANT: MEDICAID	0.051	0.727
PAYMENTSOURCE_AT_TRANSPLANT: MEDICARE	0.072	0.699
PAYMENTSOURCE_AT_TRANSPLANT: SOME PRIVATE BY PRIMARY OR SECONDARY	0.052	0.741

Table A-10: Additional model testing. 10 random samples of 80,000 training observations and 20,000 out-of-sample observations. **Donor variables that were removed: AGE_DON, COD_CAD_DON, COLD_ISCH_KI, DEATH_MECH_DON, HIST_DIABETES_DON, and HIST_HYPERTENS_DON.

Model	5-year C-index	5-Year integrated Brier score
EPTS for Adult Recipients and Deceased Donors Using the Same Cross-Validation Data as the Proposed Model	0.665	Not Calculated
Proposed Model Using PMM Imputation for Adult Recipients and Deceased Donors and without Donor Variables**	0.689	0.078

Table A-11: Proposed model and EPTS model cross-validation results in Table 2-3. C-index based on 10 random samples of 80,000 training observations and 20,000 out-of-sample observations. Using a paired two sample Student's t-test, we reject the null hypothesis that the difference in model performance means is equal to 0 (p-value = $2.4 \times 10^{-}$

[11]). We also used a Shapiro-Wilk normality test and an F test for equality of variances to verify the assumptions of the t-test (Shapiro-Wilk p-value of 0.654 and 0.298 for the proposed model data and EPTS model data respectively; hence we don't reject the null hypothesis of normally distributed model performance results. F test p-value of 0.605; hence we don't reject the null hypothesis of equality of model performance variance).

Test	Proposed model	EPTS model
1	0.721	0.698
2	0.727	0.701
3	0.724	0.694
4	0.724	0.695
5	0.721	0.692
6	0.715	0.685
7	0.727	0.700
8	0.720	0.695
9	0.729	0.702
10	0.730	0.702

APPENDIX B. APPENDIX FOR CHAPTER 3

Table B-1: Summary of all the variables considered in the analysis after the initial data preparation. The mean value in the data is shown for numeric variables, and the percentage of observations for each category is shown for categorical variables. †See Table B-2 for categories in this group.

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
ABO: A	33.8%	35%	32.3%		35.4%
ABO: A1	1.1%	1.3%	0.9%		1.2%
ABO: A1B	0.1%	0.1%	0.1%		0.1%
ABO: A2	0.2%	0.2%	0.1%		0.2%
ABO: A2B	0%	<0.1%	<0.1%		<0.1%
ABO: AB	5.1%	5.2%	3.8%		4.7%
ABO: B	12.2%	13%	14.4%		13%
ABO: O	47.4%	45.2%	48.3%		45.3%
ABO_DON: A	12.8%				19.7%
ABO_DON: A1	20.6%				12%
ABO_DON: A1B	1.5%				0.8%
ABO_DON: A2	2.1%				1.6%
ABO_DON: A2B	0.4%				0.2%
ABO_DON: AB	1.6%				1.6%
ABO_DON: B	11.5%				10.6%
ABO_DON: O	49.4%				53.6%
ABO_MAT: COMPATIBLE	3.6%				10.4%
ABO_MAT: IDENTICAL	96.3%				89%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
ABO_MAT: INCOMPATIBLE	0.1%				0.5%
AGE	50.6				48.6
AGE_DON	33.4			33.5	38.7
AMIS: 0	14.4%				19.3%
AMIS: 1	37.1%				41.6%
AMIS: 2	48.5%				39.2%
ANTICONV_DON: N	94.3%				93.7%
ANTICONV_DON: Y	5.7%				6.3%
ANTIHYPE_DON: N	77.8%				81.2%
ANTIHYPE_DON: Y	22.2%				18.8%
ANY_DIAL: N	1.5%				5.8%
ANY_DIAL: Y	98.5%				94.2%
ARGININE_DON: N	45%				44.5%
ARGININE_DON: Y	55%				55.5%
BLOOD_INF_DON: 0	90.9%				92.3%
BLOOD_INF_DON: 1	9.1%				7.7%
BMI_CALC	28.1				27.3
BMI_DON_CALC	26.3				26.8
BMIS: 0	10.8%				14.8%
BMIS: 1	24.6%				33.1%
BMIS: 2	64.7%				52.1%
BUN_DON	16.6				15.3

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
CANCER_SITE_DON: NO	96%				89.9%
CANCER_SITE_DON: YES	4%				10.1%
CARDARREST_NEURO: N	89.1%				93.4%
CARDARREST_NEURO: Y	10.9%				6.6%
CLIN_INFECT_DON: N	45.6%				56.4%
CLIN_INFECT_DON: Y	54.4%				43.6%
CMV_DON: NEGATIVE	35.2%				37.3%
CMV_DON: POSITIVE	64.8%				62.7%
CMV_IGG: NEGATIVE	32.6%				34.9%
CMV_IGG: NOT DONE	0.7%				0.8%
CMV_IGG: POSITIVE	66.7%				64.2%
CMV_IGM: NEGATIVE	56.2%				58%
CMV_IGM: NOT DONE	38.8%				36%
CMV_IGM: POSITIVE	5%				6%
COD_CAD_DON: ANOXIA	35%				19.7%
COD_CAD_DON: CEREBROVASCULAR/STROKE	18.9%				36.2%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
COD_CAD_DON: CNS TUMOR	0.2%				0.6%
COD_CAD_DON: HEAD TRAUMA	43.3%				41%
COD_CAD_DON: OTHER SPECIFY	2.6%				2.4%
COLD_ISCH_KI	18.1				13.7
CREAT_DON	1.3				1.1
CREAT_TRR	8.2			8.2	8
DAYSWAIT_CHRON	903.7	869.3		895.4	671.9
DDAVP_DON: N	80%				73.6%
DDAVP_DON: Y	20%				26.4%
DEATH_CIRCUM_DON: CHILD-ABUSE	0.4%				0.7%
DEATH_CIRCUM_DON: DEATH FROM NATURAL CAUSES	18.6%				30.9%
DEATH_CIRCUM_DON: HOMICIDE	10.6%				6.3%
DEATH_CIRCUM_DON: MVA	19.8%				21.9%
DEATH_CIRCUM_DON: NON-MVA	11.2%				9.6%
DEATH_CIRCUM_DON: NONE OF THE ABOVE	22.6%				21.6%
DEATH_CIRCUM_DON: SUICIDE	16.8%				8.9%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
DEATH_MECH_DON: ASPHYXIATION	6.4%				3.3%
DEATH_MECH_DON: BLUNT INJURY	27.6%				28.2%
DEATH_MECH_DON: CARDIOVASCULAR	9.4%				9.9%
DEATH_MECH_DON: DEATH FROM NATURAL CAUSES	0.9%				1.7%
DEATH_MECH_DON: DRUG INTOXICATION	17.4%				3.7%
DEATH_MECH_DON: INTRACRANIAL HEMORRHAGE/STROKE	20.1%				37.9%
DEATH_MECH_DON: NONE OF THE ABOVE	3.1%				4.8%
DEATH_MECH_DON: STAB OR GUNSHOT WOUND	15.2%				10.6%
DIAB: NO	66%	66.6%	59%	66%	69.1%
DIAB: NOT KNOWN	1.2%	1%	1.1%	1.3%	1.3%
DIAB: YES	32.8%	32.4%	39.9%	32.7%	29.7%
DIABETES_DON: N	95.4%				95.4%
DIABETES_DON: Y	4.6%				4.6%
DIAG_KI: GROUP_1*	21%			20.7%	22%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
DIAG_KI: GROUP_2*	8.4%			8.3%	10.8%
DIAG_KI: GROUP_3*	54.2%			54.4%	43.9%
DIAG_KI: GROUP_4*	8.4%			8.2%	8.8%
DIAG_KI: GROUP_5*	7.4%			7.8%	13.9%
DIAG_KI: NOT KNOWN	0.5%			0.6%	0.7%
DIAL_TRR: N	10%				16.6%
DIAL_TRR: Y	90%				83.4%
DISTANCE	225.5				167.5
DON_RETYP: N	54.5%				62%
DON_RETYP: Y	45.5%				38%
DRMIS: 0	19.3%				21.3%
DRMIS: 1	44.8%				46.1%
DRMIS: 2	35.9%				32.6%
DRUGTRT_COPD: N	99.1%	98.8%	98.7%		99%
DRUGTRT_COPD: Y	0.9%	1.2%	1.3%		1%
EBV_SEROSTATUS: NEGATIVE	11.2%				11%
EBV_SEROSTATUS: NOT DONE	16.2%				25%
EBV_SEROSTATUS: POSITIVE	72.6%				64%
ECD_DONOR: 0	93.9%			93.8%	83.8%
ECD_DONOR: 1	6.1%			6.2%	16.2%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
END_STAT_KI: KI: ACTIVE - CRITICAL STATUS (6)	<0.1 %				0.1%
END_STAT_KI: KI: ACTIVE - MEDICALLY URGENT (5)	0.1%				0.2%
END_STAT_KI: KI: ACTIVE (1)	99.9%				97.1%
END_STAT_KI: KI: OLD TEMPORARILY INACTIVE (7)	0%				0.1%
END_STAT_KI: KI: TEMPORARILY INACTIVE (7)	0%				2.5%
ETHCAT: AMER IND/ALASKA NATIVE	0.9%	1.1%	0.9%		0.9%
ETHCAT: ASIAN	6%	6.1%	5.9%		5.2%
ETHCAT: BLACK	31.4%	30.5%	28%		26%
ETHCAT: HISPANIC	15.8%	15.6%	15.6%		14.5%
ETHCAT: MULTIRACIAL	0.6%	0.6%	0.5%		0.6%
ETHCAT: NATIVE HAWAIIAN/OTHER PACIFIC ISLANDER	0.4%	0.4%	0.5%		0.4%
ETHCAT: WHITE	45%	45.7%	48.6%		52.4%
ETHCAT_DON: AMER	0.4%				0.5%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
IND/ALASKA NATIVE					
ETHCAT_DON: ASIAN	1.1%				2.7%
ETHCAT_DON: BLACK	14.4%				13.1%
ETHCAT_DON: HISPANIC	12.4%				13.9%
ETHCAT_DON: MULTIRACIAL	0.4%				0.6%
ETHCAT_DON: NATIVE HAWAIIAN/OTHER PACIFIC ISLANDER	0.1%				0.2%
ETHCAT_DON: WHITE	71.3%				69.1%
FUNC_STAT_TCR: 10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY		0.1%	0.4%	<0.1%	<0.1%
FUNC_STAT_TCR: 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT		1.5%	2.1%	1.7%	1.1%
FUNC_STAT_TCR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING		15.7%	17.3%	16.6%	12.7%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
WITH SOME ASSISTANCE					
FUNC_STAT_TCR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE		76.2%	72.4%	75.4%	78.6%
FUNC_STAT_TCR: NOT APPLICABLE (PATIENT < 1 YEAR OLD)		0.2%	0.4%	0.2%	0.3%
FUNC_STAT_TCR: NOT KNOWN		6.4%	7.5%	6.1%	7.1%
FUNC_STAT_TRR: 10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY	0.2%				0.1%
FUNC_STAT_TRR: 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT	2.9%				2.1%
FUNC_STAT_TRR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE	23.2%				17%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
FUNC_STAT_TRR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE	70.4%				74.7%
FUNC_STAT_TRR: NOT APPLICABLE (PATIENT < 1 YEAR OLD)	<0.1 %				0.5%
FUNC_STAT_TRR: NOT KNOWN	3.3%				5.5%
GENDER: F	37.1%	40.8%	39.9%		39.6%
GENDER: M	62.9%	59.2%	60.1%		60.4%
GENDER_DON: F	29.8%				46.6%
GENDER_DON: M	70.2%				53.4%
HBV_CORE: NEGATIVE	82.1%				79.6%
HBV_CORE: NOT DONE	10%				12.6%
HBV_CORE: POSITIVE	7.9%				7.8%
HBV_CORE_DON: NEGATIVE	93.9%				91.9%
HBV_CORE_DON: NOT DONE	0.1%				4.3%
HBV_CORE_DON: POSITIVE	6%				3.8%
HBV_SUR_ANTIGEN: NEGATIVE	96.5%				96.2%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
HBV_SUR_ANTIGEN: NOT DONE	1%				1.8%
HBV_SUR_ANTIGEN: POSITIVE	2.5%				2.1%
HEP_C_ANTI_DON: CANNOT DISCLOSE	0%				<0.1%
HEP_C_ANTI_DON: INDETERMINATE	0%				<0.1%
HEP_C_ANTI_DON: NEGATIVE	99.9%				97.5%
HEP_C_ANTI_DON: NOT DONE	0.1%				0.1%
HEP_C_ANTI_DON: PENDING	0%				<0.1%
HEP_C_ANTI_DON: POSITIVE	0%				2.4%
HEPARIN_DON: N	6.2%				8.6%
HEPARIN_DON: Y	93.8%				91.4%
HGT_CM_CALC	169.7				169
HGT_CM_DON_CALC	172.4				168.9
HIST_CANCER_DON: N	98.3%				97.8%
HIST_CANCER_DON: Y	1.7%				2.2%
HIST_CIG_DON: N	71.4%				72.5%
HIST_CIG_DON: Y	28.6%				27.5%
HIST_DIABETES_DON: NO	92.9%				63%
HIST_DIABETES_DON: NOT KNOWN	2.6%				32.8%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
HIST_DIABETES_DON: YES	4.5%				4.2%
HIST_HYPERTENS_DON: N	81.1%			81%	81%
HIST_HYPERTENS_DON: Y	18.9%			19%	19%
HIST_OTH_DRUG_DON: N	35.3%				70.3%
HIST_OTH_DRUG_DON: Y	64.7%				29.7%
HLAMIS: 0	8.1%				9.8%
HLAMIS: 1	1.4%				3.3%
HLAMIS: 2	4.4%				8.4%
HLAMIS: 3	11.9%				17.6%
HLAMIS: 4	27.7%				22%
HLAMIS: 5	30.8%				25.7%
HLAMIS: 6	15.6%				13.2%
INIT_AGE		48	49.3	48.2	46.8
INIT_STAT: ACTIVE	82.5%	84.1%	80%		86.2%
INIT_STAT: INACTIVE	17.5%	15.9%	19.9%		13.8%
INIT_STAT: KI: ACTIVE - CRITICAL STATUS (6)	0%	0.1%	<0.1%		<0.1%
INOTROP_AGENTS: N	96.6%				96.7%
INOTROP_AGENTS: Y	3.4%				3.3%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
INOTROP_SUPPORT_DON: N	51.8%				43.5%
INOTROP_SUPPORT_DON: Y	48.2%				56.5%
INSULIN_DON: N	41.2%				39.9%
INSULIN_DON: Y	58.8%				60.1%
LT_KI_BIOPSY: N	65.2%				62.1%
LT_KI_BIOPSY: Y	34.8%				37.9%
MALIG: N	94.4%				94.9%
MALIG: Y	5.6%				5.1%
MALIG_TCR_KI: N	95%	95.2%	94.7%		95.4%
MALIG_TCR_KI: Y	5%	4.8%	5.3%		4.6%
MALIG_TRR: N	99.4%				99.4%
MALIG_TRR: Y	0.6%				0.6%
MED_COND_TRR: HOSPITALIZED NOT IN ICU	0.8%				1.2%
MED_COND_TRR: IN INTENSIVE CARE UNIT	0.1%				0.1%
MED_COND_TRR: NOT HOSPITALIZED	99.1%				98.7%
NON_HRT_DON: N	87.4%				89.8%
NON_HRT_DON: Y	12.6%				10.2%
NUM_PREV_TX	0.1	0.1	0.2		0.1
ON_DIALYSIS: N	21.5%	21.1%	25.6%		27.4%
ON_DIALYSIS: Y	78.5%	78.9%	74.4%		72.6%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
ON_DIALYSIS_REGISTRATION: N		14.3%	10.2%	14.9%	18%
ON_DIALYSIS_REGISTRATION: Y		85.7%	89.8%	85.1%	82%
ON_EXPAND_DONOR: 0	52.9%	50.8%			54.3%
ON_EXPAND_DONOR: 1	47.1%	49.2%			45.7%
ON_IEXPAND_DONOR: 0	58.7%	58.5%			60.4%
ON_IEXPAND_DONOR: 1	41.3%	41.5%			39.6%
ORG_REC_ON: ICE	77.5%				84.8%
ORG_REC_ON: PUMP	22.5%				15.2%
PAYMENTSOURCE_AT_TRANSPLANT: MEDICAID	5.5%				5.1%
PAYMENTSOURCE_AT_TRANSPLANT: MEDICARE	61.7%				45.5%
PAYMENTSOURCE_AT_TRANSPLANT: OTHER	1.5%				1.8%
PAYMENTSOURCE_AT_TRANSPLANT: SOME PRIVATE BY PRIMARY OR SECONDARY	31.3%				47.6%
PERIP_VASC: N	96%	95.9%	95%		96.4%
PERIP_VASC: Y	4%	4.1%	5%		3.6%
PREV_KI_TX: N	88%				88.2%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
PREV_KI_TX: Y	12%				11.8%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: MEDICAID		8%	7.4%		7.2%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: MEDICARE		39.5%	38.4%		32.6%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: OTHER		2.9%	2.7%		2.8%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: SOME PRIVATE BY PRIMARY OR SECONDARY		49.5%	51.5%		57.4%
PROTEIN_URINE: N	54.8%				63.5%
PROTEIN_URINE: Y	45.2%				36.5%
PT_DIURETICS_DON: N	42.9%				45.7%
PT_DIURETICS_DON: Y	57.1%				54.3%
PT_STEROIDS_DON: N	30.8%				28.7%
PT_STEROIDS_DON: Y	69.2%				71.3%
PT_T3_DON: N	99%				98.5%
PT_T3_DON: Y	1%				1.5%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
PT_T4_DON: N	43.3%				48.3%
PT_T4_DON: Y	56.7%				51.7%
PULM_INF_DON: 0	56.4%				67.2%
PULM_INF_DON: 1	43.6%				32.8%
PUMP_KI: N	60.1%				71.6%
PUMP_KI: Y	39.9%				28.4%
REGION: 1	4.2%	3.7%	3.7%		4.1%
REGION: 2	13.4%	11.9%	14.3%		14.3%
REGION: 3	10.1%	15.2%	12.9%		12.8%
REGION: 4	8%	9%	9.8%		8.6%
REGION: 5	14.9%	15.8%	18.5%		16.2%
REGION: 6	3.5%	3.7%	2.7%		3.4%
REGION: 7	9.9%	7.4%	9.3%		9.7%
REGION: 8	7.3%	6.9%	5%		6.1%
REGION: 9	8.5%	6.9%	7.4%		7%
REGION: 10	9.8%	8.2%	7.7%		8.5%
REGION: 11	10.4%	11.1%	8.8%		9.4%
RT_KI_BIOPSY: N	64.6%				61.6%
RT_KI_BIOPSY: Y	35.4%				38.4%
SGOT_DON	159.8				118
SGPT_DON	153.4				100.2
SHARE_TY: 3	73.2%				82%
SHARE_TY: 4	10.5%				5.5%
SHARE_TY: 5	16.3%				12.5%
SHARE_TY: 6	0%				<0.1%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
TATTOOS: N	50.3%				75.3%
TATTOOS: Y	49.7%				24.7%
TBILI_DON	1				1
TOT_SERUM_ALBUM	3.9	3.9	3.8		3.9
TX_PROCEDUR_TY_KI: EN-BLOC	1%				1.2%
TX_PROCEDUR_TY_KI: LEFT KIDNEY	45.4%				59.2%
TX_PROCEDUR_TY_KI: RIGHT KIDNEY	53.3%				38.8%
TX_PROCEDUR_TY_KI: SEQUENTIAL KIDNEY	0.4%				0.8%
TXKID: E	1.3%				2%
TXKID: L	45.4%				59.2%
TXKID: R	53.3%				38.8%
URINE_INF_DON: 0	90.7%				90.8%
URINE_INF_DON: 1	9.3%				9.2%
VASODIL_DON: N	87.1%				87.5%
VASODIL_DON: Y	12.9%				12.5%
VDRL_DON: CANNOT DISCLOSE	0%				<0.1%
VDRL_DON: NEGATIVE	96.7%				98.7%

Table B-1 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
VDRL_DON: NOT DONE	2.1%				0.7%
VDRL_DON: POSITIVE	1.2%				0.5%
WAITLIST_YEAR	2006.8	2006.3	2007.2		2005.2
YEAR	2009.3				2007

Table B-2: Coefficients of original categories for kidney diagnosis and their new grouping. Controlled for: recipient age, diabetes, functional status, and donor age. We used the following method to group the variable values: (1) Create binary variables (dummy variables) corresponding to each of the values for the categorical variable. (2) Build a Cox proportional hazards model to predict recipient post-transplant survival using the binary variables from step 2, in addition to other relevant variables to control for, such as recipient age. (3) Sort the coefficients for the binary variables corresponding to the categorical variable from the Cox model into a prespecified number of quantiles, representing the new categorical variable values. Note that the Cox model used to group the variable values was trained on the entire dataset, and we did not exclude HCV positive recipients, nor donors with HCV antibody, HCV RNA, and HCV RIBA status.

Factor Level	Coefficient	New Group
THIN BASEMENT MEMBRANE DISEASE	-1.893	Group 1
IGA NEPHROPATHY	-0.644	Group 1
LYMPHOMA	-0.581	Group 1
GOODPASTURE'S SYNDROME	-0.552	Group 1
ALPORT'S SYNDROME	-0.526	Group 1

Table B-2 continued

Factor Level	Coefficient	New Group
FAMILIAL NEPHROPATHY	-0.495	Group 1
DYSPLASIA	-0.457	Group 1
POLYCYSTIC KIDNEYS	-0.453	Group 1
GOUT	-0.452	Group 1
HIV NEPHROPATHY	-0.337	Group 1
MEDULLARY CYSTIC DISEASE	-0.330	Group 1
RAPID PROGRESSIVE GLOMERULONEPHRITIS (RPGN)	-0.329	Group 1
FOCAL GLOMERULAR SCLEROSIS (FOCAL SEGMENTAL - FSG)	-0.179	Group 1
LITHIUM TOXICITY	-0.176	Group 1
ANTI-GBM	-0.174	Group 1
MEMBRANOUS GLOMERULONEPHRITIS	-0.142	Group 2
CHRONIC PYELONEPHRITIS/REFLUX NEPHROPATH	-0.130	Group 2
SARCOIDOSIS	-0.112	Group 2
IDIO/POST-INF CRESCENTIC GLOMERULONEPHRI	-0.103	Group 2
CONGENITAL OBSTRUCTIVE UROPATHY	-0.082	Group 2
NEPHROLITHIASIS	-0.079	Group 2
CHRONIC GLOMERULONEPHRITIS UNSPECIFIED	-0.074	Group 2
POLYARTERITIS	-0.069	Group 2
WEGENERS GRANULOMATOSIS	-0.060	Group 2
HENOCH-SCHOENLEIN PURPURA	-0.041	Group 2
NEPHROPHTHISIS	-0.034	Group 2
NEPHRITIS	-0.007	Group 2
RHEUMATOID ARTHRITIS	-0.006	Group 2
MESANGIO-CAPILLARY 1 GLOMERULONEPHRITIS	-0.004	Group 2
ACQUIRED OBSTRUCTIVE NEPHROPATHY	0.000	Group 2
MESANGIO-CAPILLARY 2 GLOMERULONEPHRITIS	0.008	Group 3
PROGRESSIVE SYSTEMIC SCLEROSIS	0.011	Group 3
DIABETES MELLITUS - TYPE OTHER / UNKNOWN	0.018	Group 3

Table B-2 continued

Factor Level	Coefficient	New Group
MEMBRANOUS NEPHROPATHY	0.039	Group 3
CHRONIC NEPHROSCLEROSIS-UNSPECIFIED	0.073	Group 3
MALIGNANT HYPERTENSION	0.080	Group 3
DRUG RELATED INTERSTITIAL NEPHRITIS	0.084	Group 3
UROLITHIASIS	0.089	Group 3
DIABETES MELLITUS - TYPE II	0.090	Group 3
CHRONIC GLOMERULOSCLEROSIS UNSPECIFIED	0.093	Group 3
HEROIN NEPHROTOXICITY	0.107	Group 3
ACUTE TUBULAR NECROSIS	0.116	Group 3
OTHER SPECIFY	0.120	Group 3
HYPERTENSIVE NEPHROSCLEROSIS	0.123	Group 3
SYSTEMIC LUPUS ERYTHEMATOSUS	0.124	Group 4
ANTIBIOTIC-INDUCED NEPHRITIS	0.126	Group 4
ANALGESIC NEPHROPATHY	0.129	Group 4
DIABETES MELLITUS - TYPE I	0.175	Group 4
CORTICAL NECROSIS	0.196	Group 4
RENAL CELL CARCINOMA	0.197	Group 4
OXALATE NEPHROPATHY (INCLUDES HEREDITARY OXALOSIS)	0.215	Group 4
HYPOPLASIA/DYSPLASIA/DYSGENSIS/AGENESIS	0.273	Group 4
HEMOLYTIC UREMIC SYNDROME	0.282	Group 4
WILMS' TUMOR	0.296	Group 4
PRUNE BELLY SYNDROME	0.299	Group 4
PRE-BMTRANSPLANTATION TOTAL BODY IRRADIATION	0.327	Group 4
CHOLESTEROL EMBOLIZATION	0.333	Group 4
INCIDENTAL CARCINOMA	0.359	Group 4
MYELOMA	0.362	Group 4
RETRANSPLANT/GRAFT FAILURE	0.363	Group 5
RENAL ARTERY THROMBOSIS	0.402	Group 5
HEPATORENAL SYNDROME	0.412	Group 5

Table B-2 continued

Factor Level	Coefficient	New Group
DIABETES - TYPE II NON-INSULIN DEP/ADULT	0.414	Group 5
DIABETES - TYPE I NON-INSULIN DEP/JUV ON	0.455	Group 5
DIABETES - TYPE II INSULIN DEP/ADULT ONS	0.461	Group 5
CANCER CHEMOTHERAPY INDUCED NEPHRITIS	0.485	Group 5
DIABETES - TYPE I INSULIN DEP/JUV ONSET	0.490	Group 5
CYSTINOSIS	0.531	Group 5
FABRY'S DISEASE	0.541	Group 5
CALCINEURIN INHIBITOR NEPHROTOXICITY	0.692	Group 5
AMYLOIDOSIS	0.727	Group 5
SCLERODERMA	0.748	Group 5
RADIATION NEPHRITIS	0.837	Group 5
SICKLE CELL ANEMIA	1.161	Group 5

Table B-3: Description of variables used in predictive models. †See Table B-2 for categories in this group.

Variable Name	Description	Categories
AGE	Recipient age (yrs)	NA
AGE_DON	Donor age (yrs)	NA
CREAT_TRR	Recipient serum creatinine at time of transplant	NA
DAYSWAIT_CHRON	Total days on waiting list including inactive time	NA
DIAB	Recipient diabetes at registration	NO, NOT_KNOWN, YES
DIAG_KI	Kidney recipient primary diagnosis at transplant	GROUP_1†, GROUP_2†, GROUP_3†, GROUP_4†,

Table B-3 continued

Variable Name	Description	Categories
		GROUP_5†, NOT_KNOWN
DIAL_TRR	Recipient pretransplant dialysis (y,n) at transplant	NO, YES
ECD_DONOR	ECD donor	0, 1
ETHCAT	Recipient ethnicity category	AMER IND/ALASKA NATIVE, ASIAN, BLACK, HISPANIC, MULTIRACIAL, NATIVE HAWAIIAN/OTHER PACIFIC ISLANDER, WHITE
FUNC_STAT_TCR	Recipient functional status at registration	10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY, 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT, 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE, 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE, NOT APPLICABLE (PATIENT < 1 YEAR OLD), NOT_KNOWN

Table B-3 continued

Variable Name	Description	Categories
FUNC_STAT_TRR	Recipient functional status at transplant	10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY, 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT, 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE, 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE, NOT APPLICABLE (PATIENT < 1 YEAR OLD), NOT_KNOWN
HIST_HYPERTENS_DON	Deceased donor-history of hypertension (y,n)	NO, YES
INIT_AGE	Candidate age in years at time of listing	NA
ON_DIALYSIS	Candidate on dialysis? (waitlist most recent)	NO, YES
ON_DIALYSIS_REGISTRATION	Recipient was on dialysis prior to waitlist registration. This was calculated by taking the difference between the date placed on the waitlist (INIT_DATE from the UNOS data) and the date first placed on dialysis (we used the minimum of DIALYSIS_DATE and DIAL_DATE as the date first	NO, YES

Table B-3 continued

Variable Name	Description	Categories
	placed on dialysis). If we had both (1) missing data from the dates, and (2) both DIAL_TCR and DIAL_TRR were set to 'No', we set the value of ON_DIALYSIS_REGISTRATION to be zero. Negative values were also set to zero.	
ON_EXPAND_DONOR	Accept local expanded donor kidney?	0, 1
ON_IEXPAND_DONOR	Accept imported expanded donor kidney?	0, 1
PERIP_VASC	Recipient peripheral vascular disease at registration	NO, YES
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION	Recipient primary payment source at registration	MEDICAID, MEDICARE, OTHER, SOME PRIVATE BY PRIMARY OR SECONDARY
REGION	UNOS region where transplanted	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11
TOT_SERUM_ALBUM	Recipient total serum albumin at registration	NA
WAITLIST_YEAR	Date placed on waiting list	NA

Table B-4: Variables with the top 10 permutation importance. Variables also selected by Lasso are marked with an †.

IRD	Waitlist	Non-IRD
AGE_DON†	DIAB†	DAYSWAIT_CHRON†
AGE†	ETHCAT†	DIAB†
CREAT_TRR†	FUNC_STAT_TCR†	ETHCAT†
DIAB†	INIT_AGE†	INIT_AGE†
DIAG_KI†	ON_DIALYSIS†	ON_DIALYSIS†
ECD_DONOR†	PERIP_VASC†	ON_EXPAND_DONOR†

Table B-4 continued

IRD	Waitlist	Non-IRD
HIST_HYPERTENSDON†	PROJECTED_PAYMENTSOURCE_AT_REGISTRATION	ON_IEXPAND_DONOR†
ON_DIALYSIS†	REGION†	PERIP_VASC†
ON_EXPAND_DONOR	TOT_SERUM_ALBUM†	TOT_SERUM_ALBUM†
ON_IEXPAND_DONOR	WAITLIST_YEAR†	WAITLIST_YEAR†

Table B-5: Performance of predictive models. Performance based on 10 random samples of 80% training data and 20% out-of-sample validation data. When preforming imputation in the out-of-sample data when cross-validating our predictive models, we did not use the response variable (patient survival time and censored status) in the imputation. For the waitlist kidney model, we used a random sample of 80,000 training observations and 20,000 out-of-sample validation observations, instead of using 80% and 20% of all waitlist records.

Model	C Index at 5 Years	5 Year Integrated Brier Score	Standard Deviation of C Index	Standard Deviation of Integrated Brier Score
IRD Organ	0.690	0.064	0.023	0.006
Non-IRD Organ	0.698	0.068	0.007	0.001
Waitlist	0.688	0.101	0.005	0.001

Table B-6: Example of using the benefit equation.

Variable values:	DIAL_TRR:Y=1, PERIP_VASC:Y=0, DIAB:YES=0, ON_EXPAND_DONOR:1=0, ETHCAT:WHITE=1, DIAB:NOT KNOWN=0, ON_IEXPAND_DONOR:1=0, PROJECTED_PAYMENTSOURCE_AT_REGISTRATION:MEDICARE=0, CREAT_TRR=7.991, AGE=48.607, WAITLISTDAYS=671.879, AGE_DON=38.697, REGION:5=1, REGION:3=0, FUNC_STAT_TRR:80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE=1,

Table B-6 continued

	WAITLIST_YEAR=2005.174, ETHCAT:HISPANIC=0, PROJECTED_PAYMENTSOURCE_AT_REGISTRATION:SOME PRIVATE BY PRIMARY OR SECONDARY=1, FUNC_STAT_TRR:NOT KNOWN=0, HIST_HYPERTENS_DON:Y=0, DIAG_KI:GROUP_3=1, TOT_SERUM_ALBUM=3.893, ECD_DONOR:1=0, DIAG_KI:GROUP_5=0
Equation output (IRD organ benefit):	4.12 (A potential recipient with these variable values is predicted to have a 4.12% higher survival probability receiving an IRD kidney than waiting for a non-IRD kidney for the specified wait time)

APPENDIX C. APPENDIX FOR CHAPTER 4

Table C-1: Coefficients of original categories for patient diagnosis and their new grouping. Controlled for: recipient age, diabetes, functional status, and donor age. We used the following method to group the variable values: (1) Create binary variables (dummy variables) corresponding to each of the values for the categorical variable. (2) Build a Cox proportional hazards model to predict recipient post-transplant survival using the binary variables from step 2, in addition to other relevant variables to control for, such as recipient age. (3) Sort the coefficients for the binary variables corresponding to the categorical variable from the Cox model into a prespecified number of quantiles, representing the new categorical variable values. Note that the Cox model used to group the variable values was trained on the entire dataset, and we did not exclude HCV positive recipients, nor donors with HCV antibody, HCV RNA, and HCV RIBA status.

Organ	Factor level	Coefficient	New group
Heart	RESTRICTIVE MYOPATHY: ENDOCARDIAL FIBROS	-0.870	Group 1
	RESTRICTIVE MYOPATHY: SARCOIDOSIS	-0.734	Group 1
	RESTRICTIVE MYOPATHY: OTHER SPECIFY	-0.456	Group 1
	HYPERTROPHIC CARDIOMYOPATHY	-0.393	Group 1
	DILATED MYOPATHY: VIRAL	-0.359	Group 1
	DILATED MYOPATHY: FAMILIAL	-0.353	Group 1
	CONGENITAL HEART DEFECT - WITHOUT SURGERY	-0.252	Group 1
	DILATED MYOPATHY: MYOCARDITIS	-0.241	Group 2
	DILATED MYOPATHY: OTHER SPECIFY	-0.229	Group 2
	DILATED MYOPATHY: IDIOPATHIC	-0.148	Group 2
	VALVULAR HEART DISEASE	-0.137	Group 2
	OTHER - SPECIFY	-0.080	Group 2
	RESTRICTIVE MYOPATHY: IDIOPATHIC	-0.072	Group 2
	DILATED MYOPATHY: ADRIAMYCIN	-0.015	Group 3
	CORONARY ARTERY DISEASE	-0.009	Group 3
	CANCER	0.000	Group 3
	DILATED MYOPATHY: ISCHEMIC	0.028	Group 3

Table C-1 continued

	CONGENITAL HEART DEFECT - PRIOR SURGERY UNKNOWN	0.182	Group 3
	HEART RE-TX/GF: NON-SPECIFIC	0.188	Group 3
	DILATED MYOPATHY: ALCOHOLIC	0.230	Group 4
	HEART RE-TX/GF: CORONARY ARTERY DISEASE	0.236	Group 4
	HEART RE-TX/GF: CHRONIC REJECTION	0.254	Group 4
	HEART RE-TX/GF: ACUTE REJECTION	0.349	Group 4
	CONGENITAL HEART DEFECT - WITH SURGERY	0.368	Group 4
	CONGENITAL HEART DEFECT - HYPOPLASTIC LEFT HEART SYNDROME - UNOPERATED	0.377	Group 4
	DILATED MYOPATHY: POST PARTUM	0.405	Group 5
	RESTRICTIVE MYOPATHY: AMYLOIDOSIS	0.493	Group 5
	HEART RE-TX/GF: RESTRICTIVE/CONSTRICTIVE	0.609	Group 5
	HEART RE-TX/GF: OTHER SPECIFY	0.743	Group 5
	RESTRICTIVE MYOPATHY: SEC TO RADIAT/CHEM	0.753	Group 5
	HEART RE-TX/GF: PRIMARY FAILURE	0.857	Group 5
	HEART RE-TX/GF: HYPERACUTE REJECTION	1.438	Group 5
Liver	BENIGN TUMOR: HEPATIC ADENOMA	-11.543	Group 1
	METDIS: MAPLE SYRUP URINE DISEASE	-2.096	Group 1
	BILIARY HYPOPLASIA: NONSYNDROMIC PAUCITY OF INTRAHEPATIC BILE DUCT	-0.909	Group 1
	METDIS: WILSON'S DISEASE, OTHER COPPER METABOLISM DISORDER	-0.709	Group 1
	AHN: TYPE A	-0.709	Group 1
	METDIS: TYROSINEMIA	-0.591	Group 1
	PSC: ULCERATIVE COLITIS	-0.493	Group 1
	BILIARY ATRESIA: EXTRAHEPATIC	-0.437	Group 1

Table C-1 continued

	PSC: NO BOWEL DISEASE	-0.433	Group 1
	CONGENITAL HEPATIC FIBROSIS	-0.431	Group 1
	METDIS: ALPHA-1-ANTITRYPSIN DEFIC A-1-A	-0.379	Group 1
	CIRRHOSIS: TYPE B- HBSAG+	-0.372	Group 1
	AHN: TYPE B- HBSAG+	-0.332	Group 1
	PRIMARY BILIARY CIRRHOSIS (PBC)	-0.274	Group 1
	CIRRHOSIS: DRUG/INDUST EXPOSURE OTHER SPECIFY	-0.263	Group 1
	PSC: CROHN'S DISEASE	-0.249	Group 2
	BENIGN TUMOR: POLYCYSTIC LIVER DISEASE	-0.249	Group 2
	BILIARY HYPOPLASIA: ALAGILLE SYNDROME (PAUCITY OF INTRAHEPATIC BILE DUCT)	-0.245	Group 2
	CIRRHOSIS: FATTY LIVER (NASH)	-0.210	Group 2
	CIRRHOSIS: CRYPTOGENIC (IDIOPATHIC)	-0.186	Group 2
	FAMILIAL CHOLESTASIS: OTHER SPECIFY	-0.173	Group 2
	METDIS: GLYC STOR DIS TYPE I (GSD-I)	-0.167	Group 2
	CIRRHOSIS: CHRONIC ACTIVE HEPATITIS: ETIOLOGY UNKNOWN	-0.167	Group 2
	AHN: TYPE B AND D	-0.115	Group 2
	FAMILIAL CHOLESTASIS: BYLER'S DISEASE	-0.109	Group 2
	CIRRHOSIS: TYPE A	-0.071	Group 2
	METDIS: GLYC STOR DIS TYPE IV (GSD-IV)	-0.069	Group 2
	BUDD-CHIARI SYNDROME	-0.065	Group 2
	BILIARY ATRESIA OR HYPOPLASIA: OTHER, SPECIFY	-0.062	Group 2
	ALCOHOLIC CIRRHOSIS	-0.060	Group 3
	CIRRHOSIS: AUTOIMMUNE	-0.049	Group 3
	AHN: DRUG OTHER SPECIFY	-0.044	Group 3
	SEC BILIARY CIRRHOSIS: CAROLI'S DISEASE	-0.044	Group 3
	AHN: OTHER, SPECIFY (E.G., ACUTE VIRAL INFECTION,	-0.018	Group 3

Table C-1 continued

	AUTOIMMUNE HEPATITIS - FULMINANT)		
	CIRRHOSIS: TYPE B AND D	-0.007	Group 3
	ACUTE ALCOHOLIC HEPATITIS	0.000	Group 3
	AHN: ETIOLOGY UNKNOWN	0.023	Group 3
	PSC: OTHER SPECIFY	0.036	Group 3
	CHOLES LIVER DISEASE: OTHER SPECIFY	0.097	Group 3
	BENIGN TUMOR: OTHER SPECIFY	0.111	Group 3
	METDIS: HEMOCHROMATOSIS - HEMOSIDEROSIS	0.151	Group 3
	AHN: TYPE D	0.164	Group 3
	CIRRHOSIS: OTHER, SPECIFY (E.G., HISTIOCYTOSIS, SARCOIDOSIS, GRANULOMATOUS)	0.168	Group 3
	METDIS: OTHER SPECIFY	0.194	Group 4
	CIRRHOSIS: TYPE B AND C	0.200	Group 4
	ALCOHOLIC CIRRHOSIS WITH HEPATITIS C	0.209	Group 4
	PLM: HEPATOMA (HCC) AND CIRRHOSIS	0.220	Group 4
	PLM: HEMANGIOENDOTHELIOMA, HEMANGIOSARCOMA, ANGIOSARCOMA	0.226	Group 4
	PLM: HEPATOMA - HEPATOCELLULAR CARCINOMA	0.228	Group 4
	TPN/HYPERALIMENTATION IND LIVER DISEASE	0.242	Group 4
	SECONDARY HEPATIC MALIGNANCY OTHER SPECIFY	0.243	Group 4
	CIRRHOSIS: TYPE C	0.257	Group 4
	OTHER SPECIFY	0.312	Group 4
	SEC BILIARY CIRRHOSIS: CHOLEDOCHOL CYST	0.338	Group 4
	NEONATAL CHOLESTATIC LIVER DISEASE	0.353	Group 4
	AHN: TYPE B AND C	0.367	Group 4
	NEONATAL HEPATITIS OTHER SPECIFY	0.373	Group 4
	AHN: TYPE C	0.398	Group 5

Table C-1 continued

	CIRRHOSIS: CRYPTOGENIC-IDIOPATHIC	0.458	Group 5
	METDIS: HYPERLIPIDEMIA-II, HOMOZYGOUS HYPERCHOLESTEROLEMIA	0.495	Group 5
	SEC BILIARY CIRRHOSIS: OTHER SPECIFY	0.535	Group 5
	CYSTIC FIBROSIS	0.612	Group 5
	CIRRHOSIS: TYPE D	0.667	Group 5
	GRAFT FAILURE	0.706	Group 5
	PLM: OTHER SPECIFY (I.E., KLATZKIN TUMOR, LEIOMYSARCOMA)	0.725	Group 5
	METDIS: PRIMARY OXALOSIS/OXALURIA, HYPEROXALURIA	0.730	Group 5
	TRAUMA OTHER SPECIFY	0.735	Group 5
	PLM: HEPATOBLASTOMA (HBL)	0.781	Group 5
	PLM: CHOLANGIOCARCINOMA (CH-CA)	0.804	Group 5
	GRAFT VS. HOST DIS SEC TO NON-LI TX	0.849	Group 5
	PLM: FIBROLAMELLAR (FL-HC)	0.851	Group 5
	BILE DUCT CANCER: (CHOLANGIOMA, BILIARY TRACT CARCINOMA)	1.107	Group 5
Lung	CARCINOID TUMORLETS	-13.775	Group 1
	HERMANSKY PUDLAK SYNDROME	-13.696	Group 1
	FIBROCAVITARY LUNG DISEASE	-13.690	Group 1
	KARTAGENER'S SYNDROME	-13.633	Group 1
	EISENMENGER'S SYN: PDA	-13.537	Group 1
	FIBROSING MEDIASTINITIS	-13.482	Group 1
	SCHWACKMAN-DIAMOND SYNDROME	-13.461	Group 1
	PORTOPULMONARY HYPERTENSION	-13.379	Group 1
	CONGENITAL MALFORMATION	-13.298	Group 1
	LYMPHANGIOLEIOMYOMATOSIS	-0.772	Group 1
	SILICOSIS	-0.661	Group 1
	CREST - PULMONARY HYPERTENSION	-0.627	Group 1
	EISENMENGER'S SYN: ATRIAL SEPTAL DEFEC	-0.583	Group 1

Table C-1 continued

	IDIOPATHIC PULMONARY HEMOSIDEROSIS	-0.569	Group 1
	HYPOGAMMAGLOBULINEMIA	-0.548	Group 1
	BRONCHOPULMONARY DYSPLASIA	-0.527	Group 1
	SCLERODERMA	-0.502	Group 2
	GRANULOMATOUS LUNG DISEASE	-0.376	Group 2
	HYPERSENSITIVITY PNEUMONITIS	-0.322	Group 2
	ALPHA - 1 - ANTITRYPSIN DEFICIENCY	-0.320	Group 2
	WEGENER'S GRANULOMA - BRONCHIECTASIS	-0.296	Group 2
	ALVEOLAR PROTEINOSIS	-0.291	Group 2
	SARCOIDOSIS	-0.260	Group 2
	PULMONARY VASCULAR DISEASE	-0.242	Group 2
	OTHER - SPECIFY	-0.230	Group 2
	BRONCHIECTASIS	-0.212	Group 2
	COPD/EMPHYSEMA	-0.190	Group 2
	CYSTIC FIBROSIS	-0.189	Group 2
	SJOGREN'S SYNDROME	-0.182	Group 2
	RHEUMATOID DISEASE	-0.152	Group 2
	OBSTRUCTIVE LUNG DISEASE	-0.152	Group 2
	IDIOPATHIC PULMONARY FIBROSIS / USUAL INTERSTITIAL PNEUMONITIS	-0.146	Group 2
	OBLITERATIVE BRONCHIOLITIS (NON-RETRANSP	-0.142	Group 3
	SURFACTANT PROTEIN B DEFICIENCY	-0.106	Group 3
	EOSINOPHILIC GRANULOMA	-0.100	Group 3
	BOOP	-0.076	Group 3
	PULMONARY FIBROSIS OTHER SPECIFY CAUSE	-0.067	Group 3
	SCLERODERMA - PULMONARY HYPERTENSION	-0.064	Group 3
	PRIMARY PULMONARY HYPERTENSION	-0.054	Group 3
	OCCUPATIONAL LUNG DISEASE OTHER SPECIFY	-0.016	Group 3

Table C-1 continued

	ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS	0.000	Group 3
	CHRONIC PNEUMONITIS OF INFANCY	0.003	Group 3
	SCLERODERMA - RESTRICTIVE	0.055	Group 3
	SECONDARY PULMONARY HYPERTENSION	0.063	Group 3
	ARDS/PNEUMONIA	0.099	Group 3
	LYMPHOCYTIC INTERSTITIAL PNEUMONITIS	0.105	Group 3
	PULMONARY VENO-OCCLUSIVE DISEASE	0.163	Group 3
	MIXED CONNECTIVE TISSUE DISEASE	0.171	Group 4
	LUNG RE-TX/GF: OBLITERATIVE BRONCHIOLITIS-OBSTRUCTIVE	0.192	Group 4
	CONSTRICTIVE BRONCHIOLITIS	0.218	Group 4
	LUNG RE-TX/GF: NON-SPECIFIC	0.228	Group 4
	POLYMYOSITIS	0.266	Group 4
	LUNG RE-TX/GF: OBLITERATIVE BRONCHIOLITIS-RESTRICTIVE	0.274	Group 4
	LUNG RE-TX/GF: OBLITERATIVE BRONCHIOLITI	0.287	Group 4
	PULMONARY THROMBOEMBOLIC DISEASE	0.325	Group 4
	LUPUS	0.331	Group 4
	LUNG RE-TX/GF: OBSTRUCTIVE	0.356	Group 4
	GRAFT-VS-HOST DISEASE (GVHD)	0.379	Group 4
	LUNG RE-TX/GF: PRIMARY GRAFT FAILURE	0.570	Group 4
	PULMONARY TELENGECTASIA - RESTRICTIVE	0.665	Group 4
	INHALATION BURNS/TRAUMA	0.690	Group 4
	BRONCHOALVEOLAR CARCINOMA (BAC)	0.729	Group 4
	LUNG RE-TX/GF: OTHER SPECIFY	0.732	Group 4
	PULMONARY HYALINIZING GRANULOMA	0.780	Group 5
	WEGENER'S GRANULOMA - RESTRICTIVE	0.800	Group 5
	LUNG RE-TX/GF: ACUTE REJECTION	0.801	Group 5

Table C-1 continued

	EHLERS-DANLOS SYNDROME	0.810	Group 5
	PRIMARY CILIARY DYSKINESIA	0.910	Group 5
	COMMON VARIABLE IMMUNE DEFICIENCY	1.015	Group 5
	PULMONARY TELENGECTASIA - PULMONARY HYPERTENSION	1.024	Group 5
	EISENMENGER'S SYN: OTHER SPECIFY	1.336	Group 5
	LUNG RE-TX/GF: RESTRICTIVE	1.568	Group 5
	TUBEROUS SCLEROSIS	1.570	Group 5
	SWYER JAMES SYNDROME	1.697	Group 5
	CREST - RESTRICTIVE	1.789	Group 5
	EISENMENGER'S SYN: MULTI CONGENITAL ANOM	1.948	Group 5
	EISENMENGER'S SYN: VSD	2.128	Group 5
	PULMONIC STENOSIS	2.389	Group 5
	THROMBOEMBOLIC PULMONARY HYPERTENSION	2.586	Group 5

Table C-2: Description of variables used in predictive models. *See Table C-1 for categories in this group.

Variable Name	Description	Categories
AGE	Recipient age (yrs)	NA
AGE_DON	Donor age (yrs)	NA
ASCITES_TX	Recipient ascites at transplant	ABSENT, MODERATE, SLIGHT
BMI_CALC	Calculated recipient bmi	NA
CIG_USE	History of cigarette use	NO, YES
CREAT_TRR	Recipient serum creatinine at time of transplant	NA
DAYSWAIT_CHRON	Total days on waiting list	NA
DEATH_MECH_DON	Deceased donor-mechanism of death	ASPHYXIATION, BLUNT INJURY, CARDIOVASCULAR, DEATH FROM

Table C-2 continued

Variable Name	Description	Categories
		NATURAL CAUSES, DRUG INTOXICATION, INTRACRANIAL HEMORRHAGE/STROKE, NONE OF THE ABOVE, STAB OR GUNSHOT WOUND
DGN_TCR	Primary diagnosis at time of listing	GROUP_1*, GROUP_2*, GROUP_3*, GROUP_4*, GROUP_5*, NOT_KNOWN
DIAB	Recipient diabetes at registration	NO, NOT_KNOWN, YES
DIAG	Recipient primary diagnosis	GROUP_1*, GROUP_2*, GROUP_3*, GROUP_4*, GROUP_5*
ECMO_TCR	Patient on life support - ecmo at registration	0, 1
ETHCAT	Recipient ethnicity category	AMER IND/ALASKA NATIVE, ASIAN, BLACK, HISPANIC, MULTIRACIAL, NATIVE HAWAIIAN/OTHER PACIFIC ISLANDER, WHITE
EXC_HCC	Type of exception relative to hcc: hbl, hcc,non-hcc: hbl=hepatoblastoma	HCC, NON-HCC

Table C-2 continued

Variable Name	Description	Categories
FINAL_DIALYSIS_PRIOR_WEEK	Most recent waiting list dialysis twice in prior week or at removal if removed	A, NO, YES
FUNC_STAT_TCR	Recipient functional status at registration	10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY, 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT, 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE, 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE, NOT APPLICABLE (PATIENT < 1 YEAR OLD), NOT_KNOWN
FUNC_STAT_TRR	Recipient functional status at transplant	10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY, 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT

Table C-2 continued

Variable Name	Description	Categories
		IMMINENT, 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE, 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE, NOT APPLICABLE (PATIENT < 1 YEAR OLD), NOT_KNOWN
GROUPING	Lu/hl diagnosis grouping on wl(on thoracic_dgn/tcr_tgn/trr_dgn)	A, B, C, D
HGT_CM_DON_CALC	Calculated donor height (cm)	NA
HGT_CM_TCR	Recipient height at registration	NA
HIST_CIG_DON	Deceased donor-history of cigarettes in past at >20pack yrs	NO, YES
INIT_AGE	Age in years at time of listing	NA
INIT_ALBUMIN	Initial waiting list albumin	NA
INIT_BILIRUBIN	Initial waiting list bilirubin	NA
INIT_BLU_FLG	Lung preference at listing - both (1=y)	0, 1
INIT_INR	Initial waiting list inr	NA
INIT_MELD_OR_PELD	Initial waiting list use meld or peld	MELD, PELD
INIT_O2	O2 requirement at rest at tcr/listing	NA
INIT_RLU_FLG	Lung preference at listing - right (1=y)	0, 1
INIT_SERUM_CREAT	Initial waiting list serum creatinine	NA

Table C-2 continued

Variable Name	Description	Categories
INIT_STAT	Initial waiting list status code	LU: ACTIVE, LU: TEMPORARILY INACTIVE
INOTROPES_TCR	IB inotropes at registration	0, 1
INSULIN_DON	Deceased donor-was donor given insulin within 24 hrs pre cross clamp?	NO, YES
LIFE_SUP	Recipient life support calculated on tcr_life_sup and vad_device_ty	NO, YES
LIFE_SUP_TCR	Recipient life support at registration	NO, YES
LIFE_SUP_TRR	Recipient life support pre-transplant at transplant	NO, YES
MED_COND_TRR	Recipient medical condition pre-transplant at transplant	HOSPITALIZED NOT IN ICU, IN INTENSIVE CARE UNIT, NOT HOSPITALIZED
MOST_RCNT_CREAT	Recipient most recent absolute creatinine at registration	NA
NUM_PREV_TX	The number of previous transplants	NA
ON_VENT_TRR	Recipient on ventilator at transplant	0, 1
PAYMENTSOURCE_AT_TRANSPLANT	Recipient primary payment source at transplant	MEDICAID, MEDICARE, OTHER, SOME PRIVATE BY PRIMARY OR SECONDARY
PREV_AB_SURG_TCR	Recipient previous upper abdominal surgery at registration	NO, YES
PRIOR_CARD_SURG_TCR	Tcr prior cardiac surgery at listing (non-transplant)	NO, YES
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION	Recipient primary payment source at registration	MEDICAID, MEDICARE, OTHER, SOME PRIVATE BY

Table C-2 continued

Variable Name	Description	Categories
		PRIMARY OR SECONDARY
REGION	Wl unos/optn region where listed/transplanted	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11
SGPT_DON	Deceased donor-terminal sgpt/alt	NA
THORACIC_DGN	Waitlist candidate diagnosis	GROUP_1*, GROUP_2*, GROUP_3*, GROUP_4*, GROUP_5*, NOT_KNOWN
TOT_SERUM_ALBUM	Recipient total serum albumin at registration	NA
TRANSFUSIONS	Events occurring between listing and transplant: transfusions y/n/u	NO, YES
VAD_DEVICE_TY_TCR	Candidate type of vad device at listing	
VENTILATOR_TCR	Patient on life support - ventilator at registration	0, 1
WAITLIST_YEAR	Date placed on waiting list	NA

Table C-3: Variables with the top 10 permutation importance. Variables also selected by Lasso are marked with an *.

Organ	IRD	Non-IRD	Waitlist
Heart	AGE_DON*	CIG_USE*	ECMO_TCR*
	AGE*	DAYSWAIT_CHRON*	FUNC_STAT_TCR*
	CREAT_TRR*	ETHCAT*	HGT_CM_TCR*
	DEATH_MECH_DON*	INIT_AGE*	INIT_STAT*
	DIAG*	MOST_RCNT_CREAT*	INOTROPES_TCR*
	FUNC_STAT_TRR*	PRIOR_CARD_SURG_TCR*	LIFE_SUP*
	INSULIN_DON*	PROJECTED_PAYMENTSOURC	MOST_RCNT_CREAT*

Table C-3 continued

Organ	IRD	Non-IRD	Waitlist
		E_AT_REGISTRATION	
	MOST_RCNT_CREAT*	THORACIC_DGN*	VAD_DEVICE_TY_TCR*
	PAYMENTSOURCE_AT_TRANSPLANT	TOT_SERUM_ALBUM*	VENTILATOR_TCR*
	TRANSFUSIONS*	WAITLIST_YEAR*	WAITLIST_YEAR*
Liver	AGE*	DGN_TCR*	EXC_HCC*
	ASCITES_TX*	DIAB*	FUNC_STAT_TCR*
	BMI_CALC*	FUNC_STAT_TCR*	INIT_ALBUMIN*
	FINAL_DIALYSIS_PRIOR_WEEK*	INIT_AGE*	INIT_BILIRUBIN*
	FUNC_STAT_TRR*	INIT_MELD_OR_PELD*	INIT_INR*
	INIT_SERUM_CREAT*	INIT_MELD_PELD_LAB_SCORE	INIT_SERUM_CREAT*
	LIFE_SUP_TRR*	INIT_SERUM_CREAT*	INIT_STAT*
	MED_COND_TRR*	NUM_PREV_TX*	LIFE_SUP_TCR*
	ON_VENT_TRR*	PREV_AB_SURG_TCR*	VENTILATOR_TCR*
	SGPT_DON*	PROJECTED_PAYMENTSOURCE_AT_REGISTRATION	WAITLIST_YEAR*
Lung	AGE*	FUNC_STAT_TCR*	CIG_USE*
	BMI_CALC	GROUPING*	FUNC_STAT_TCR*
	DIAG*	INIT_AGE*	GROUPING*
	GROUPING*	INIT_BLU_FLG*	INIT_O2*
	HGT_CM_DON_CALC*	INIT_CREAT	INIT_RLU_FLG*
	HIST_CIG_DON*	INIT_O2*	LIFE_SUP
	ISCHTIME	NUM_PREV_TX	REGION*
	MED_COND_TRR	PROJECTED_PAYMENTSOURC	THORACIC_DGN*

Table C-3 continued

Organ	IRD	Non-IRD	Waitlist
		E_AT_REGISTRATION	
	REGION	REGION*	VENTILATOR_TCR
	STEROID	THORACIC_DGN*	WAITLIST_YEAR*

Table C-4: Summary of all the variables used in the predictive models for the heart and their distribution in the general heart transplant population in the data. The mean value in the data is shown for numeric variables, and the percentage of observations for each category is shown for categorical variables. *See Table C-1 for categories in this group.

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
AGE	49.4				45.1
AGE_DON	27.9			27.9	28.1
CIG_USE: N	56.1%	59.9%			59.7%
CIG_USE: Y	43.9%	40.1%			40.3%
CREAT_TRR	1.2			1.2	1.2
DAYSWAIT_CHRON	192.1	179.9		190.5	190.7
DEATH_MECH_DON: ASPHYXIATION	5.7%			5.3%	3.6%
DEATH_MECH_DON: BLUNT INJURY	32.5%			32.8%	37.8%
DEATH_MECH_DON: CARDIOVASCULAR	4.8%			4.7%	5.4%

Table C-4 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
DEATH_MECH_DON: DEATH FROM NATURAL CAUSES	0.5%			0.5%	1.3%
DEATH_MECH_DON: DRUG INTOXICATION	17.2%			17.3%	4%
DEATH_MECH_DON: INTRACRANIAL HEMORRHAGE/STROKE	12.3%			12.5%	24.2%
DEATH_MECH_DON: NONE OF THE ABOVE	3.7%			3.6%	5.6%
DEATH_MECH_DON: STAB OR GUNSHOT WOUND	23.3%			23.3%	18.1%
DIAG: GROUP_1*	7.2%				7.3%
DIAG: GROUP_2*	42.5%				42.7%
DIAG: GROUP_3*	39.8%				38.6%
DIAG: GROUP_4*	7.1%				8.7%
DIAG: GROUP_5*	3.4%				2.7%

Table C-4 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
ECMO_TCR: 0	98.7%	98.6%	97.5%		98.6%
ECMO_TCR: 1	1.3%	1.4%	2.5%		1.4%
ETHCAT: AMER IND/ALASKA NATIVE	0.1%	0.3%	0.3%		0.3%
ETHCAT: ASIAN	3.1%	3.2%	2.6%		2.9%
ETHCAT: BLACK	18.4%	19.4%	19.2%		18.2%
ETHCAT: HISPANIC	8%	9.5%	9.1%		8.8%
ETHCAT: MULTIRACIAL	0.8%	0.9%	0.8%		0.8%
ETHCAT: NATIVE HAWAIIAN/ OTHER PACIFIC ISLANDER	0.3%	0.3%	0.3%		0.3%
ETHCAT: WHITE	69.1%	66.5%	67.6%		68.7%
FUNC_STAT_TCR: 10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY		19.2%	15.4%	19.8%	14.4%
FUNC_STAT_TCR: 30-50 PERCENT		24.9%	19.4%	26.7%	19.5%

Table C-4 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT					
FUNC_STAT_TCR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE		30%	30%	29.8%	30.6%
FUNC_STAT_TCR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE		14.9%	14.6%	16.8%	14.9%
FUNC_STAT_TCR: NOT APPLICABLE (PATIENT < 1 YEAR OLD)		9%	18.1%	4.9%	18.2%

Table C-4 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
FUNC_STAT_TCR: NOT KNOWN		2%	2.4%	2%	2.3%
FUNC_STAT_TRR: 10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY	23.7%				17%
FUNC_STAT_TRR: 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT	28.6%				20.8%
FUNC_STAT_TRR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE	25%				23.8%

Table C-4 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
FUNC_STAT_TRR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE	17.3%				17.7%
FUNC_STAT_TRR: NOT APPLICABLE (PATIENT < 1 YEAR OLD)	3.2%				17.7%
FUNC_STAT_TRR: NOT KNOWN	2.2%				3%
HGT_CM_TCR		162.9	162.8		163.7
INIT_AGE		44.2	44.3	48.7	44.6
INIT_STAT: HR: OLD STATUS 1	0%	<0.1%	0%		0.1%
INIT_STAT: HR: STATUS 1A	28.3%	29.1%	28.1%		28%
INIT_STAT: HR: STATUS 1B	35%	34.6%	31.2%		32.5%
INIT_STAT: HR: STATUS 2	34.9%	34.1%	38.1%		37.6%

Table C-4 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
INIT_STAT: HR: TEMPORARILY INACTIVE	1.8%	2.2%	2.6%		1.9%
INOTROPES_TCR: 0	66.1%	63.2%	63.7%		62.1%
INOTROPES_TCR: 1	33.9%	36.8%	36.3%		37.9%
INSULIN_DON: N	39.5%			39.8%	36.7%
INSULIN_DON: Y	60.5%			60.2%	63.3%
LIFE_SUP: N	45.8%	45.7%	47.2%		46.7%
LIFE_SUP: Y	54.2%	54.3%	52.8%		53.3%
MOST_RCNT_CREAT	1.2	1.2	1.3	1.2	1.2
PAYMENTSOURCE_AT_TRANSPLANT: MEDICAID	12.5%				16.4%
PAYMENTSOURCE_AT_TRANSPLANT: MEDICARE	27.8%				20.8%
PAYMENTSOURCE_AT_TRANSPLANT: OTHER	4.9%				4.9%
PAYMENTSOURCE_AT_TRANSPLANT: SOME	54.8%				57.9%

Table C-4 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
PRIVATE BY PRIMARY OR SECONDARY					
PRIOR_CARD_SURG_TCR: N	60%	61.5%			61.1%
PRIOR_CARD_SURG_TCR: Y	40%	38.5%			38.9%
PROJECTED_PAYMENT SOURCE_AT_REGISTRATION: MEDICAID		16.8%	16.5%	12.6%	16.1%
PROJECTED_PAYMENT SOURCE_AT_REGISTRATION: MEDICARE		20.8%	19.9%	23.6%	18.5%
PROJECTED_PAYMENT SOURCE_AT_REGISTRATION: OTHER		5.3%	5.4%	5.2%	5.5%
PROJECTED_PAYMENT SOURCE_AT_REGISTRATION: SOME PRIVATE BY		57%	58.1%	58.6%	59.9%

Table C-4 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
PRIMARY OR SECONDARY					
THORACIC_DGN: GROUP_1*		7.8%	7%	7.4%	7.3%
THORACIC_DGN: GROUP_2*		43.9%	41.7%	43.9%	42.7%
THORACIC_DGN: GROUP_3*		35.2%	38.1%	38.6%	39%
THORACIC_DGN: GROUP_4*		10.4%	9.9%	7.2%	8.4%
THORACIC_DGN: GROUP_5*		2.8%	3.2%	3%	2.6%
TOT_SERUM_ALBUM	3.7	3.7			3.6
TRANSFUSIONS: N	78%			77.5%	74.3%
TRANSFUSIONS: Y	22%			22.5%	25.7%
VAD_DEVICE_TY_TCR: LVAD		13.4%	11.8%		11.3%
VAD_DEVICE_TY_TCR: LVAD/RVAD/TAH UNSPECIFIED		0.4%	2.6%		2.7%
VAD_DEVICE_TY_TCR:		2.4%	2.1%		2%

Table C-4 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
LVAD+RVAD					
VAD_DEVICE_TY_TCR: NONE		83.3%	83.1%		83.7%
VAD_DEVICE_TY_TCR: RVAD		0.1%	0.1%		0.1%
VAD_DEVICE_TY_TCR: TAH		0.4%	0.3%		0.3%
VENTILATOR_TCR: 0	96.6%	95.1%	92.8%		94.7%
VENTILATOR_TCR: 1	3.4%	4.9%	7.2%		5.3%
WAITLIST_YEAR	2008.8	2008.3	2007.3		2006.7

Table C-5: Summary of all the variables used in the predictive models for the liver and their distribution in the general liver transplant population in the data. The mean value in the data is shown for numeric variables, and the percentage of observations for each category is shown for categorical variables. *See Table C-1 for categories in this group.

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
AGE	49.4				49

Table C-5 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
ASCITES_TX: ABSENT	22.3%			23.3%	24.2%
ASCITES_TX: MODERATE	28.9%			28.5%	26.8%
ASCITES_TX: SLIGHT	48.8%			48.2%	49%
BMI_CALC	27.7			27.9	27.3
DAYSWAIT_CHRON	240.2	217.1		251.1	248.7
DGN_TCR: GROUP_1*		22.2%	12.5%		14.6%
DGN_TCR: GROUP_2*		21.7%	12%		10.6%
DGN_TCR: GROUP_3*		33.1%	21.7%		20.3%
DGN_TCR: GROUP_4*		19.2%	49.1%		49.3%
DGN_TCR: GROUP_5*		3.8%	4.7%		5.1%
DGN_TCR: NOT KNOWN		<0.1%	<0.1%		0.1%
DIAB: NO	73.8%	76.5%	75.6%		77.5%
DIAB: NOT KNOWN	1.4%	1.3%	2%		2.1%
DIAB: YES	24.8%	22.2%	22.4%		20.4%
EXC_HCC: HCC	14.7%	12.7%	12.6%		19.3%
EXC_HCC: NON-HCC	85.3%	87.3%	87.4%		80.7%
FINAL_DIALYSIS_PRIOR_WEEK: A	0.4%			0.3%	4.2%
FINAL_DIALYSIS_PRIOR_WEEK: N	89.9%			91.1%	89.6%

Table C-5 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
FINAL_DIALYSIS_PRIOR_WEEK: Y	9.7%			8.7%	6.2%
FUNC_STAT_TCR: 10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY		13.5%	8.1%	10.9%	8.1%
FUNC_STAT_TCR: 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT		14.4%	11.2%	14.9%	10.7%
FUNC_STAT_TCR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE		25%	26.3%	28.5%	25.3%
FUNC_STAT_TCR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE		36.2%	41.7%	37.6%	42.2%

Table C-5 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
FUNC_STAT_TCR: NOT APPLICABLE (PATIENT < 1 YEAR OLD)		6.2%	7.9%	3.5%	8.4%
FUNC_STAT_TCR: NOT KNOWN		4.6%	4.8%	4.6%	5.3%
FUNC_STAT_TRR: 10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY	21.5%				13%
FUNC_STAT_TRR: 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT	25.2%				17%
FUNC_STAT_TRR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE	23.2%				24.9%
FUNC_STAT_TRR: 80-100 PERCENT PERFORMS	23.8%				31.3%

Table C-5 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE					
FUNC_STAT_TRR: NOT APPLICABLE (PATIENT < 1 YEAR OLD)	3.7%				9.7%
FUNC_STAT_TRR: NOT KNOWN	2.6%				4.2%
INIT_AGE		46	49.4	50.9	48.3
INIT_ALBUMIN	3	3	3		3
INIT_BILIRUBIN	8.4	8.3	6.1		6.8
INIT_INR	1.9	1.9	1.7		1.8
INIT_MELD_OR_PELD: MELD	94.2%	88.8%	93.5%		92.3%
INIT_MELD_OR_PELD: PELD	5.8%	11.2%	6.5%		7.7%
INIT_SERUM_CREAT	1.3	1.2	1.3	1.3	1.2
INIT_STAT: <= 10		20.9%	25.2%		27.8%
INIT_STAT: >= 25		20.3%	15%		15.2%
INIT_STAT: 11-18		33.9%	38.7%		35%
INIT_STAT: 1A		6.6%	3.2%		3.4%
INIT_STAT: 1B		0.3%	0.1%		0.1%
INIT_STAT: 24-19		16.9%	14.5%		14.1%

Table C-5 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
INIT_STAT: 2A		<0.1%	0.3%		0.3%
INIT_STAT: 2B		0.2%	1.6%		2.9%
INIT_STAT: NOT KNOWN		0%	0%		0.1%
INIT_STAT: TEMPORARILY INACTIVE		1%	1.4%		1.2%
LIFE_SUP_TCR: N	94.2%	94.3%	95%	95.7%	95.6%
LIFE_SUP_TCR: Y	5.8%	5.7%	5%	4.3%	4.4%
LIFE_SUP_TRR: N	90%				92.3%
LIFE_SUP_TRR: Y	10%				7.7%
MED_COND_TCR: HOSPITALIZED NOT IN ICU				13.9%	11.4%
MED_COND_TCR: IN INTENSIVE CARE UNIT				10.7%	9.4%
MED_COND_TCR: NOT HOSPITALIZED				75.4%	79.2%
MED_COND_TRR: HOSPITALIZED NOT IN ICU	20.2%				16.8%
MED_COND_TRR: IN INTENSIVE CARE UNIT	17.6%				14.1%
MED_COND_TRR: NOT	62.2%				69.1%

Table C-5 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
HOSPITALIZED					
NUM_PREV_TX	0.1	0.1	0.1		0.1
ON_VENT_TRR: 0	91.5%			93.6%	93.5%
ON_VENT_TRR: 1	8.5%			6.4%	6.5%
PREV_AB_SURG_TCR: N	59.7%	59.2%	60%		60.5%
PREV_AB_SURG_TCR: Y	40.3%	40.8%	40%		39.5%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: MEDICAID		16.8%	16.3%		16%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: MEDICARE		14.8%	16.1%		13.6%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: OTHER		5.3%	5.6%		6.1%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: SOME PRIVATE BY PRIMARY OR SECONDARY		63.1%	61.9%		64.3%
SGPT_DON	100.9			108.3	68.7

Table C-5 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
VENTILATOR_TCR: 0	94.5%	94.7%	95.5%		96%
VENTILATOR_TCR: 1	5.5%	5.3%	4.5%		4%
WAITLIST_YEAR	2008.6	2008.1	2007.3		2006.5

Table C-6: Summary of all the variables used in the predictive models for the lung and their distribution in the general lung transplant population in the data. The mean value in the data is shown for numeric variables, and the percentage of observations for each category is shown for categorical variables. *See Table C-1 for categories in this group.

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
AGE	53.8				52.8
CIG_USE: N			42.5%		40.4%
CIG_USE: Y			57.5%		59.6%
DAYSWAIT_CHRON	219.7	222.1		219.7	227.3
DIAG: GROUP_1*	1%				1.3%
DIAG: GROUP_2*	84%				82.8%
DIAG: GROUP_3*	9.5%				10.9%

Table C-6 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
DIAG: GROUP_4*	5.3%				4.7%
DIAG: GROUP_5*	0.2%				0.4%
FUNC_STAT_TCR: 10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY		5.5%	7.2%	6.2%	5.4%
FUNC_STAT_TCR: 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT		27.2%	26.5%	30.3%	26.4%
FUNC_STAT_TCR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE		49.5%	49.7%	47.7%	49.7%
FUNC_STAT_TCR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY		16%	14.6%	14.6%	16.7%

Table C-6 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
LIVING WITH NO ASSISTANCE					
FUNC_STAT_TCR: NOT APPLICABLE (PATIENT < 1 YEAR OLD)		0.7%	0.9%	0.4%	0.8%
FUNC_STAT_TCR: NOT KNOWN		1%	1%	0.9%	1%
FUNC_STAT_TRR: 10-20 PERCENT VERY SICK HOSPITALIZATION NECESSARY	11.1%				9.5%
FUNC_STAT_TRR: 30-50 PERCENT REQUIRES CONSIDERABLE ASSISTANCE BUT DEATH NOT IMMINENT	39.2%				34.5%
FUNC_STAT_TRR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME	37.9%				40.5%

Table C-6 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
ASSISTANCE					
FUNC_STAT_TRR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE	10.2%				12.8%
FUNC_STAT_TRR: NOT APPLICABLE (PATIENT < 1 YEAR OLD)	0.2%				0.8%
FUNC_STAT_TRR: NOT KNOWN	1.4%				1.9%
GROUPING: A	35.7%	32%	31.2%	37.5%	33.3%
GROUPING: B	2.2%	3.6%	4.9%	2.2%	3.5%
GROUPING: C	13.3%	13.3%	13.1%	12.7%	13.3%
GROUPING: D	48.8%	51.1%	50.8%	47.6%	49.8%
HGT_CM_DON_CALC	173.9			173.8	170.7
HIST_CIG_DON: N	83.8%			83%	88.1%
HIST_CIG_DON: Y	16.2%			17%	11.9%
INIT_AGE		52.1	51.6	53.3	52.2

Table C-6 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
INIT_BLU_FLG: 0	25.2%	25.3%	22.1%		25.5%
INIT_BLU_FLG: 1	74.8%	74.7%	77.9%		74.5%
INIT_O2	3.9	3.8	4		3.7
INIT_RLU_FLG: 0	61.8%	60.8%	64.2%		61.2%
INIT_RLU_FLG: 1	38.2%	39.2%	35.8%		38.8%
PROJECTED_PAYMENT SOURCE_AT_REGISTRATION: MEDICAID		8.4%	8.9%		8.3%
PROJECTED_PAYMENT SOURCE_AT_REGISTRATION: MEDICARE		27%	27.3%		26.6%
PROJECTED_PAYMENT SOURCE_AT_REGISTRATION: OTHER		3.8%	3.6%		3.7%
PROJECTED_PAYMENT SOURCE_AT_REGISTRATION: SOME PRIVATE BY PRIMARY OR		60.8%	60.2%		61.5%

Table C-6 continued

Variable	M_{IRD}	$M_{Non\text{-}IRD}$	M_{Wait}	M'_{IRD}	General population (including both IRD and non-IRD donors, without removing HCV positive donors or recipients)
SECONDARY					
REGION: 1	2%	2.8%	3%		2.6%
REGION: 2	12.9%	11.6%	15.5%		15.8%
REGION: 3	10.3%	12.4%	12.2%		11.4%
REGION: 4	13.8%	12.2%	11.6%		11.6%
REGION: 5	13.8%	15.7%	14.5%		14.5%
REGION: 6	3%	3.2%	3%		3%
REGION: 7	9.7%	8%	7.9%		8.2%
REGION: 8	8.2%	7.6%	7%		7%
REGION: 9	1.9%	4%	3.8%		3.6%
REGION: 10	11.3%	11.6%	11.6%		11.1%
REGION: 11	13.3%	10.8%	9.8%		11.2%
THORACIC_DGN: GROUP_1*		1.3%	1.4%	1%	1.3%
THORACIC_DGN: GROUP_2*		80.7%	78.1%	83%	81.1%
THORACIC_DGN: GROUP_3*		12.8%	14%	10%	12.4%
THORACIC_DGN: GROUP_4*		4.8%	6%	5.6%	4.9%
THORACIC_DGN: GROUP_5*		0.3%	0.5%	0.4%	0.3%
THORACIC_DGN: NOT KNOWN		<0.1%	<0.1%	0%	<0.1%
WAITLIST_YEAR	2008.8	2008.3	2008.8		2008.2

Table C-7: Performance of predictive models. Performance based on 10 random samples of 80% training data and 20% out-of-sample validation data. For the waitlist liver model, we used a random sample of 80,000 training observations and 20,000 out-of-sample validation observations, instead of using 80% and 20% of all waitlist records.

Model	Random survival forests				Cox proportional hazards model			
	5 Year C Index	5 Year Integrated Brier Score	σ C Index	σ Integrated Brier Score	5 Year C Index	5 Year Integrated Brier Score	σ C Index	σ Integrated Brier Score
IRD heart	0.646	0.114	0.029	0.008	0.641	0.118	0.030	0.011
Non-IRD heart	0.589	0.126	0.009	0.003	0.591	0.126	0.008	0.003
Waitlist heart	0.740	0.159	0.007	0.003	0.749	0.161	0.006	0.002
IRD liver	0.571	0.120	0.027	0.005	0.593	0.120	0.039	0.005
Non-IRD liver	0.620	0.117	0.008	0.002	0.622	0.117	0.007	0.002
Waitlist liver	0.777	0.144	0.007	0.002	0.804	0.142	0.005	0.002
IRD lung	0.589	0.181	0.020	0.014	0.596	0.182	0.023	0.012
Non-IRD lung	0.568	0.182	0.009	0.002	0.568	0.182	0.009	0.002
Waitlist lung	0.775	0.158	0.011	0.005	0.788	0.158	0.010	0.006

Table C-8: Example of using the benefit equations.

Organ	Variable values:	Equation output (IRD organ benefit):
Heart	ECMO_TCR:1=0, PAYMENTSOURCE_AT_TRANSPLANT:SOME PRIVATE BY PRIMARY OR SECONDARY=1, FUNC_STAT_TRR:NOT APPLICABLE (PATIENT < 1	7.96

Table C-8 continued

	YEAR OLD)=0, DIAG:GROUP_4=0, INSULIN_DON:Y=1, PAYMENTSOURCE_AT_TRANSPLANT:MEDICARE=0, VAD_DEVICE_TY_TCR:LVAD/RVAD/TAH UNSPECIFIED=0, MOST_RCNT_CREAT=1.19, PRIOR_CARD_SURG_TCR:Y=0, VENTILATOR_TCR:1=0, VAD_DEVICE_TY_TCR:NONE=1, CIG_USE:Y=0, LIFE_SUP:Y=1, INOTROPES_TCR:1=0, AGE=45.083, WAITLISTDAYS=190.687, HGT_CM_TCR=163.746, AGE_DON=28.073, WAITLIST_YEAR=2006.682, DEATH_MECH_DON:STAB OR GUNSHOT WOUND=0, FUNC_STAT_TRR:60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE=1, TOT_SERUM_ALBUM=3.647, DIAG:GROUP_3=0, DEATH_MECH_DON:INTRACRANIAL HEMORRHAGE/STROKE=0, INIT_STAT:HR: STATUS 1B=0, TRANSFUSIONS:Y=0, CREAT_TRR=1.201, INIT_STAT:HR: STATUS 2=1, ETHCAT:HISPANIC=0, ETHCAT:WHITE=1	
Liver	INIT_STAT:>= 25=0, EXC_HCC:NON-HCC=1, FINAL_DIALYSIS_PRIOR_WEEK:N=1, DGN_TCR:GROUP_4=1, FINAL_DIALYSIS_PRIOR_WEEK:Y=0, NUM_PREV_TX=0.084, VENTILATOR_TCR:1=0, DGN_TCR:GROUP_3=0, DIAB:YES=0, PREV_AB_SURG_TCR:Y=0, INIT_MELD_OR_PELD:PELD=0, INIT_STAT:11-18=1, INIT_SERUM_CREAT=1.18, LIFE_SUP_TRR:Y=0, INIT_INR=1.771, INIT_BILIRUBIN=6.835, AGE=48.968, WAITLISTDAYS=248.654, SGPT_DON=68.747, BMI_CALC=27.256, WAITLIST_YEAR=2006.485, DIAB:NOT KNOWN=0, PROJECTED_PAYMENTSOURCE_AT_REGISTRATION:MEDICARE=0, FUNC_STAT_TRR:60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE=0, ASCITES_TX:SLIGHT=1, MED_COND_TRR:NOT HOSPITALIZED=1, MED_COND_TRR:IN INTENSIVE CARE UNIT=0, ON_VENT_TRR:1=0, PROJECTED_PAYMENTSOURCE_AT_REGISTRATION:SOME PRIVATE BY PRIMARY OR SECONDARY=1, INIT_ALBUMIN=2.983,	9.08

Table C-8 continued

	FUNC_STAT_TRR:80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE=1, ASCITES_TX:MODERATE=0	
Lung	GROUPING:C=0, GROUPING:D=1, DIAG:GROUP_4=0, INIT_O2=3.75, REGION:4=0, HGT_CM_DON_CALC=170.704, WAITLISTDAYS=227.29, AGE=52.82, WAITLIST_YEAR=2008.183, FUNC_STAT_TRR:60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE=1, FUNC_STAT_TRR:80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE=0, CIG_USE:Y=1, PROJECTED_PAYMENTSOURCE_AT_REGISTRATION:MEDICARE=0, INIT_RLU_FLG:1=0, REGION:5=0, INIT_BLU_FLG:1=1, PROJECTED_PAYMENTSOURCE_AT_REGISTRATION:SOME PRIVATE BY PRIMARY OR SECONDARY=1, DIAG:GROUP_3=0, HIST_CIG_DON:Y=0	7.70

Table C-9: Benefit equation for the 5-year survival probability of receiving an IRD organ minus the 5-year survival probability of waiting for a non-IRD organ. The benefit equation predicts the increase (positive value) or decrease (negative value) in probability (multiplied by 100) of surviving to 5 years with an IRD organ vs. waiting for a non-IRD organ. Reference levels for heart categorical Factors: CIG_USE: No. DEATH_MECH_DON: Blunt injury. DIAG: Group_2. ECMO_TCR: 0. ETHCAT: Black. FUNC_STAT_TRR: 30-50 percent requires considerable assistance but death not imminent. INIT_STAT: Hr: status 1a. INOTROPES_TCR: 0. INSULIN_DON: No. LIFE_SUP: No. PAYMENTSOURCE_AT_TRANSPLANT: Medicaid. PRIOR_CARD_SURG_TCR: No. TRANSFUSIONS: No. VAD_DEVICE_TY_TCR: Lvad. VENTILATOR_TCR: 0. Reference levels for liver categorical Factors: ASCITES_TX: Absent. DGN_TCR: Group_1. DIAB: No. EXC_HCC: Hcc. FINAL_DIALYSIS_PRIOR_WEEK: A. FUNC_STAT_TRR: 30-50 percent requires considerable assistance but death not imminent. INIT_MELD_OR_PELD: Meld. INIT_STAT: <= 10. LIFE_SUP_TRR: No. MED_COND_TRR: Hospitalized not in icu. ON_VENT_TRR: 0. PREV_AB_SURG_TCR: No. PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: Medicaid. VENTILATOR_TCR: 0. Reference levels for lung categorical Factors: CIG_USE: No. DIAG: Group_2. FUNC_STAT_TRR: 30-50 percent requires considerable assistance but death not imminent. GROUPING: A. HIST_CIG_DON: No. INIT_BLU_FLG: 0.

INIT_RLU_FLG: 0. PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: Medicaid. REGION: 2. *See Table C-1 for categories in this group.

Organ	Variable	Coefficients	P-Values
Heart	(INTERCEPT)	2275.823	<0.01
	ECMO_TCR: 1	10.850	<0.01
	PAYMENTSOURCE_AT_TRANSPLANT : SOME PRIVATE BY PRIMARY OR SECONDARY	8.949	<0.01
	FUNC_STAT_TRR: NOT APPLICABLE (PATIENT < 1 YEAR OLD)	8.203	<0.01
	DIAG: GROUP_4*	7.824	<0.01
	INSULIN_DON: Y	7.492	<0.01
	PAYMENTSOURCE_AT_TRANSPLANT : MEDICARE	5.125	<0.01
	VAD_DEVICE_TY_TCR: LVAD/RVAD/TAH UNSPECIFIED	4.623	<0.01
	MOST_RCNT_CREAT	4.501	<0.01
	PRIOR_CARD_SURG_TCR: Y	4.469	<0.01
	VENTILATOR_TCR: 1	4.100	<0.01
	VAD_DEVICE_TY_TCR: NONE	2.422	<0.01
	CIG_USE: Y	1.992	<0.01
	LIFE_SUP: Y	0.772	<0.01
	INOTROPES_TCR: 1	0.461	<0.01
	AGE	0.108	<0.01
	WAITLISTDAYS	0.029	<0.01
	HGT_CM_TCR	-0.063	<0.01
	AGE_DON	-0.214	<0.01
	WAITLIST_YEAR	-1.125	<0.01
	DEATH_MECH_DON: STAB OR GUNSHOT WOUND	-1.299	<0.01
	FUNC_STAT_TRR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE	-1.964	<0.01
	TOT_SERUM_ALBUM	-2.334	<0.01
	DIAG: GROUP_3*	-2.862	<0.01
	DEATH_MECH_DON: INTRACRANIAL HEMORRHAGE/STROKE	-2.914	<0.01

Table C-9 continued

	INIT_STAT: HR: STATUS 1B	-3.424	<0.01
	TRANSFUSIONS: Y	-5.324	<0.01
	CREAT_TRR	-5.508	<0.01
	INIT_STAT: HR: STATUS 2	-5.688	<0.01
	ETHCAT: HISPANIC	-6.450	<0.01
	ETHCAT: WHITE	-6.629	<0.01
Liver	(INTERCEPT)	1024.296	<0.01
	INIT_STAT: >= 25	14.262	<0.01
	EXC_HCC: NON-HCC	10.852	<0.01
	FINAL_DIALYSIS_PRIOR_WEEK: N	9.019	<0.01
	DGN_TCR: GROUP_4*	7.795	<0.01
	FINAL_DIALYSIS_PRIOR_WEEK: Y	6.131	<0.01
	NUM_PREV_TX	5.147	<0.01
	VENTILATOR_TCR: 1	4.976	<0.01
	DGN_TCR: GROUP_3*	4.442	<0.01
	DIAB: YES	3.207	<0.01
	PREV_AB_SURG_TCR: Y	2.877	<0.01
	INIT_MELD_OR_PELD: PELD	1.724	<0.01
	INIT_STAT: 18-11	1.691	<0.01
	INIT_SERUM_CREAT	1.521	<0.01
	LIFE_SUP_TRR: Y	0.619	0.01
	INIT_INR	0.412	<0.01
	INIT_BILIRUBIN	0.392	<0.01
	AGE	0.207	<0.01
	WAITLISTDAYS	0.025	<0.01
	SGPT_DON	0.016	<0.01
	BMI_CALC	-0.380	<0.01
	WAITLIST_YEAR	-0.513	<0.01
	DIAB: NOT KNOWN	-1.525	<0.01
	PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: MEDICARE	-1.677	<0.01
	FUNC_STAT_TRR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE	-2.198	<0.01
	ASCITES_TX: SLIGHT	-2.324	<0.01

Table C-9 continued

	MED_COND_TRR: NOT HOSPITALIZED	-2.616	<0.01
	MED_COND_TRR: IN INTENSIVE CARE UNIT	-3.864	<0.01
	ON_VENT_TRR: 1	-3.964	<0.01
	PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: SOME PRIVATE BY PRIMARY OR SECONDARY	-4.201	<0.01
	INIT_ALBUMIN	-4.612	<0.01
	FUNC_STAT_TRR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE	-5.079	<0.01
	ASCITES_TX: MODERATE	-8.173	<0.01
Lung	(INTERCEPT)	1601.523	<0.01
	GROUPING: C	17.000	<0.01
	GROUPING: D	5.642	<0.01
	DIAG: GROUP_4*	3.707	<0.01
	INIT_O2	1.708	<0.01
	REGION: 4	1.674	<0.01
	HGT_CM_DON_CALC	0.443	<0.01
	WAITLISTDAYS	0.020	<0.01
	AGE	-0.111	<0.01
	WAITLIST_YEAR	-0.828	<0.01
	FUNC_STAT_TRR: 60-70 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH SOME ASSISTANCE	-1.590	<0.01
	FUNC_STAT_TRR: 80-100 PERCENT PERFORMS ACTIVITIES OF DAILY LIVING WITH NO ASSISTANCE	-1.687	<0.01
	CIG_USE: Y	-1.995	<0.01
	PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: MEDICARE	-2.099	<0.01
	INIT_RLU_FLG: 1	-2.436	<0.01
	REGION: 5	-4.904	<0.01
	INIT_BLU_FLG: 1	-6.337	<0.01
	PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: SOME PRIVATE BY PRIMARY OR SECONDARY	-7.477	<0.01
	DIAG: GROUP_3*	-15.121	<0.01

Table C-9 continued

	HIST_CIG_DON: Y	-15.214	<0.01

APPENDIX D. APPENDIX FOR CHAPTER 5

Table D-1: Description of the variables considered for the predictive models, and the percent of missing data per variable.

Variable name	Description	Categories	Missing percent
ABO	Recipient blood group at registration	A, A1, A1B, A2, A2B, AB, B, O, NOT_KNOWN	0%
BMI_TCR	BMI at listing	NA	5.8%
DIAB	Recipient diabetes at registration	NO, NOT_KNOWN, YES	16.3%
DIALYSIS_DAYS_TO_WAITLIST	Days on dialysis prior to registration. DIALYSIS_DAYS_TO_WAITLIST was calculated by taking the difference between the date placed on the kidney waitlist (INIT_DATE_KI from the UNOS data) and the date first placed on dialysis (we used the minimum of DIALYSIS_DATE and DIAL_DATE as the date first placed on dialysis). If we had both (1) missing data from the dates, and (2) both DIAL_TCR and DIAL_TRR were set to 'No', we set the value of DIALYSIS_DAYS_TO_WAITLIST to be zero. Negative values of DIALYSIS_DAYS_TO_WAITLIST were also set to zero.	NA	10.3%
ETHCAT	Recipient ethnicity category	AMER IND/ALASKA NATIVE, ASIAN, BLACK, HISPANIC, MULTIRACIAL, NATIVE	<0.1%

Table D-1 continued

Variable name	Description	Categories	Missing percent
		HAWAIIAN/OTHER PACIFIC ISLANDER, WHITE	
FUNC_STAT_TCR_TEN	Functional status at registration	NA	7.3%
FUNC_STAT_TRR_TEN	Functional status at transplant	NA	0%
GENDER	Recipient gender	F, M	0%
HCV_SEROSTATUS	Recipient HCV status	NEGATIVE, NOT DONE, POSITIVE	18%
HGT_CM_TCR	Recipient height at registration	NA	5.5%
INIT_AGE	Candidate age in years at time of listing	NA	0%
INIT_DAY	Day of week at registration	FRIDAY, MONDAY, SATURDAY, SUNDAY, THURSDAY, TUESDAY, WEDNESDAY	0%
INIT_MONTH	Day of month at registration	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12	0%
INIT_STAT	Initial waiting list status code	ACTIVE, INACTIVE, KI: ACTIVE - CRITICAL STATUS (6)	<0.1%
MALIG_TCR_KI	Recipient previous malig. at registration (kidney)	NO, YES	18.6%
NUM_PREV_TX	The number of previous transplants	NA	0%
ON_DIALYSIS	Candidate on dialysis? (y/n)	NO, YES	8.6%
PERIP_VASC	Recipient peripheral vascular disease at registration	NO, YES	19.2%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION	Recipient primary payment source at registration	MEDICAID, MEDICARE, OTHER, SOME PRIVATE BY PRIMARY OR SECONDARY	15.4%
REGION	UNOS region where transplanted	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11	0%

Table D-1 continued

Variable name	Description	Categories	Missing percent
TOT_SERUM_ALBUM	Recipient total serum albumin at registration	NA	46.4%
WAITLIST_YEAR	Date placed on waiting list	NA	0%

Table D-2: Summary statistics of the variables used in the analysis. The mean is shown for numerical variables and the percent of each category is shown for categorical variables.

Variable	Mean/Distribution
ABO: A	36.2%
ABO: A1	0.9%
ABO: A1B	0.1%
ABO: A2	0.2%
ABO: A2B	<0.1%
ABO: AB	4.7%
ABO: B	12.8%
ABO: O	45.1%
ABO: UNK	<0.1%
BMI_TCR	29.5
DIAB: NO	69.8%
DIAB: NOT KNOWN	1.1%
DIAB: YES	29.1%
DIALYSIS_DAYS_TO_WAITLIST	598.2
ETHCAT: AMER IND/ALASKA NATIVE	0.9%
ETHCAT: ASIAN	4.7%
ETHCAT: BLACK	24.9%
ETHCAT: HISPANIC	13.3%
ETHCAT: MULTIRACIAL	0.6%
ETHCAT: NATIVE HAWAIIAN/OTHER PACIFIC ISLANDER	0.4%
ETHCAT: WHITE	55.2%

Table D-2 continued

Variable	Mean/Distribution
FUNC_STAT_TCR_TEN	89.1
FUNC_STAT_TRR_TEN	87.2
GENDER: F	39.4%
GENDER: M	60.6%
HCV_SEROSTATUS: NEGATIVE	91%
HCV_SEROSTATUS: NOT DONE	3.4%
HCV_SEROSTATUS: POSITIVE	5.6%
HGT_CM_TCR	169
INIT_AGE	45.5
INIT_DAY: FRIDAY	24%
INIT_DAY: MONDAY	16.3%
INIT_DAY: SATURDAY	0.8%
INIT_DAY: SUNDAY	0.5%
INIT_DAY: THURSDAY	20.5%
INIT_DAY: TUESDAY	18.6%
INIT_DAY: WEDNESDAY	19.3%
INIT_MONTH: 01	7.9%
INIT_MONTH: 02	8%
INIT_MONTH: 03	8.9%
INIT_MONTH: 04	8.4%
INIT_MONTH: 05	8.5%
INIT_MONTH: 06	8.4%
INIT_MONTH: 07	8.3%
INIT_MONTH: 08	8.7%
INIT_MONTH: 09	8.2%
INIT_MONTH: 10	9%
INIT_MONTH: 11	8%
INIT_MONTH: 12	7.9%
INIT_STAT: ACTIVE	88.6%
INIT_STAT: INACTIVE	11.3%
INIT_STAT: KI: ACTIVE - CRITICAL STATUS (6)	0.1%
MALIG_TCR_KI: N	95.7%

Table D-2 continued

Variable	Mean/Distribution
MALIG_TCR_KI: Y	4.3%
NUM_PREV_TX	0.1
ON_DIALYSIS: N	40.7%
ON_DIALYSIS: Y	59.3%
PERIP_VASC: N	96.3%
PERIP_VASC: Y	3.7%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: MEDICAID	7.2%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: MEDICARE	33%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: OTHER	2.7%
PROJECTED_PAYMENTSOURCE_AT_REGISTRATION: SOME PRIVATE BY PRIMARY OR SECONDARY	57.2%
REGION: 1	4.4%
REGION: 2	14.1%
REGION: 3	12%
REGION: 4	8.7%
REGION: 5	16.2%
REGION: 6	3.2%
REGION: 7	10.2%
REGION: 8	6.1%
REGION: 9	7%
REGION: 10	9%
REGION: 11	9.2%
TOT_SERUM_ALBUM	3.9
WAITLIST_YEAR	2001.8

Table D-3: The original values of functional status that come with the data and the values we grouped them into, for this analysis.

Grouped Values	Original Values
10	10% - Moribund, fatal processes progressing rapidly

Table D-3 continued

Grouped Values	Original Values
10	10% - No play; does not get out of bed
20	20% - Very sick, hospitalization necessary: active treatment necessary
20	20% - Often sleeping; play entirely limited to very passive activities
30	30% - Severely disabled: hospitalization is indicated, death not imminent
30	30% - In bed; needs assistance even for quiet play
40	40% - Disabled: requires special care and assistance
40	40% - Mostly in bed; participates in quiet activities
50	Performs activities of daily living with TOTAL assistance.
50	50% - Requires considerable assistance and frequent medical care
50	50% - Can dress but lies around much of day; no active play; can take part in quiet play/activities
60	Performs activities of daily living with SOME assistance.
60	60% - Requires occasional assistance but is able to care for needs
60	60% - Up and around, but minimal active play; keeps busy with quieter activities
70	70% - Cares for self: unable to carry on normal activity or active work
70	70% - Both greater restriction of and less time spent in play activity
80	80% - Normal activity with effort: some symptoms of disease
80	80% - Active, but tires more quickly
90	90% - Able to carry on normal activity: minor symptoms of disease
90	90% - Minor restrictions in physically strenuous activity
100	Performs activities of daily living with NO assistance.
100	100% - Normal, no complaints, no evidence of disease
100	100% - Fully active, normal

Table D-4: Cross-Validation RMSE results for the model with the lowest RMSE compared to the benchmark model for each cross-validation sample.

Cross-validation sample	Permutation importance interactions: generalized additive model	Benchmark
1	13.06	14.68
2	13.09	14.69
3	13.02	14.74
4	12.99	14.63
5	13.03	14.73
6	13.01	14.69
7	13.02	14.72
8	13.07	14.64
9	12.99	14.66
10	13.04	14.66
11	13.03	14.73
12	13.06	14.77
13	13.1	14.55
14	13.06	14.57
15	13.03	14.61
16	13.01	14.67
17	13.11	14.65
18	13.06	14.85
19	13.14	14.71
20	13.01	14.68

Table D-5: Performance results from cross-validations per model, averaged for all variable selection methods. The results of the final model, GA-PIRF, were excluded from this table.

Model	RMSE	MSE	Accuracy of classification within one increment	Accuracy of classification within two increments
generalized additive model	13.17	173.58	81.42%	92.21%
Box-Cox linear regression	13.54	183.3	81.08%	91.99%
linear regression	13.59	184.58	82.7%	90.83%
neural networks	13.62	185.47	80.61%	91.37%
random forests	14.68	216.9	77.24%	89.45%
support vector machines	14.68	216.99	79.25%	89.48%
gradient boosting	14.74	218.99	77.51%	89.49%
stacking using linear regression	14.74	219.18	77.59%	89.54%
gradient boosting (classification)	16.31	267.62	78.13%	85.61%

Table D-6: Performance results from cross-validations per variable selection method, averages across all models. The results of the final model, GA-PIRF, were excluded from this table.

Variable selection method	RMSE	MSE	Accuracy of classification within one increment	Accuracy of classification within two increments
Permutation importance top 10	13.45	181.05	81.93%	91.5%
Permutation importance interactions	13.93	195.1	80.59%	90.76%
Lasso	14.25	204.11	80.01%	90.12%
MARS	15.01	227.68	77.41%	88.82%

Table D-6 continued

Variable selection method	RMSE	MSE	Accuracy of classification within one increment	Accuracy of classification within two increments
MARS interactions	15.06	229.06	77.58%	88.77%

Table D-7: Optimal tuning parameters for each model, averaged over all cross-validation samples. Note that for random forests, a 'splitrule' value of 2 is 'variance' and a 'splitrule' value of 1 is 'maxstat'.

Neural networks	Random forests	Gradient boosting	Gradient boosting (classification)	Support vector machines
size: 52.75	mtry: 8.14	nrounds: 156	nrounds: 800	gamma: 3.4
decay: 18.53	splitrule: 1.63	max_depth: 16.4	max_depth: 8.4	lambda: 8.20e-05
	min.node.size: 28.9	eta: 0.09	eta: 0.13	
		gamma: 0	gamma: 0	
		colsample_bytree: 1	colsample_bytree: 1	
		min_child_weight: 9.1	min_child_weight: 4.6	
		subsample: 1	subsample: 1	

Text D-1: Code for R to build the predictive model with the lowest RMSE and make predictions on new data.

```
library(mgcv)

load('transplant_data.RDA') #Data


#train model
```

```
model_formula = as.formula(FUNC_STAT_TRR_ten ~ FUNC_STAT_TCR_ten +
        s(WAITLIST_YEAR, k = -1, bs = "cs") +
        s(INIT_AGE, k = -1, bs = "cs") +
        s(dialysis_days_to_waitlist, k = -1, bs = "cs") +
        REGION +
        s(HGT_CM_TCR, k = -1, bs = "cs") +
        projected_paymentsource_at_registration +
        DIAB +
        s(BMI_TCR, k = -1, bs = "cs") +
        s(WAITLIST_YEAR, by = REGION, k = -1, bs = "cs")  +
        FUNC_STAT_TCR_ten:WAITLIST_YEAR +
        FUNC_STAT_TCR_ten:TOT_SERUM_ALBUM)
model <- gam(model_formula, data = Data, family=gaussian())
#use model to predict new data (in this example, we take a random observation and change
#a few variables)
prediction_data = Data[1,]
prediction_data$INIT_AGE=40
```

```
prediction_data$DIAB = 'No'

prediction_data$REGION = '3'

round(predict(model, newdata = prediction_data),-1)
```

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